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(71) Applicant *(for all designated States except US)*: MURO PHARMACEUTICAL, INC. [US/US]; 890 East Street, Tewksbury, MA 01876 (US).

(72) Inventor; and
(75) Inventor/Applicant *(for US only)*: THEOHARIDES, Theoharis, C. [US/US]; 14 Parkman Street, Brookline, MA 62146 (US).

(74) Agents: MELOY, Sybil et al.; Foley & Lardner, Suite 500, 3000 K Street, N.W., Washington, DC 20007-5109 (US).

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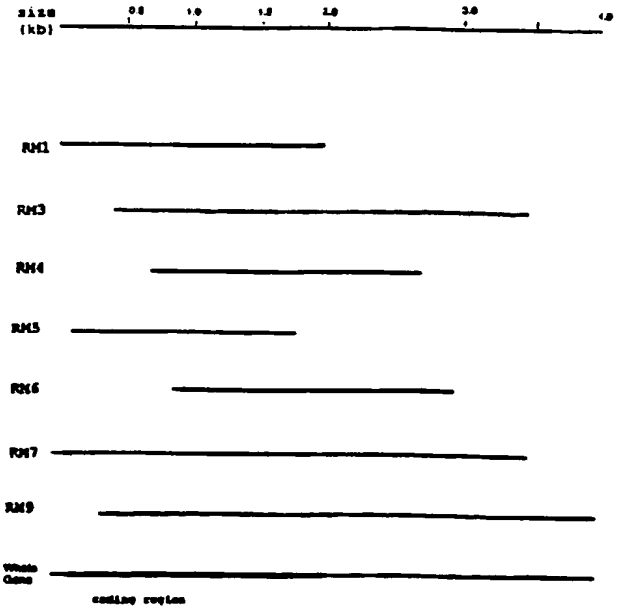
(54) Title: ISOLATED AND CLONED MAST CELL 78 kDa PHOSPHOPROTEIN (MAST CELL DEGRANULATION INHIBITORY AGENT) AND USE THEREOF

(57) Abstract

A 78 kDa mast cell protein (moesin) has been cloned from rats, and its cDNA and amino acid sequence determined. This protein is phosphorylated on specific serine and threonine residues by the action in mast cells of one or more protein kinase C isozymes, especially the ξ isozyme, thereby producing a phosphoprotein that inhibits mast cell degranulation (Mast Cell Degranulation Inhibitor Agent). *In vivo* phosphorylation of this protein in mast cells can be stimulated by drugs such as cromolyn, nedocromil, flavonoids such as quercetin and kaempherol, and lodoxamide. Mast cell degranulation can be inhibited by administration of phosphomoesin phosphatase inhibitors. Tissues deficient in mast cell moesin can be identified with a labeled anti-moesin or anti-phosphomoesin antibody and treated by transfecting such mast cells with moesin cDNA in a viral vector such as an influenza virus vector.



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ISOLATED AND CLONED MAST CELL 78 kDa PHOSPHOPROTEIN (MAST CELL DEGRANULATION INHIBITORY AGENT) AND USE THEREOF

FIELD OF THE INVENTION

The present invention provides novel proteins, along with therapeutic, diagnostic and research utilities for these proteins.

BACKGROUND OF THE INVENTION

Technology aimed at the discovery of protein factors (including e.g., cytokines, such as lymphokines, interferons, CSFs and interleukins) has matured rapidly over the past decade. The now routine hybridization cloning and expression cloning techniques clone novel polynucleotides "directly" in the sense that they rely on information directly related to the discovered protein (i.e., partial DNA/amino acid sequence of the protein in the case of hybridization cloning; activity of the protein in the case of expression cloning). More recent "indirect" cloning techniques such as signal sequence cloning, which isolates DNA sequences based on the presence of a now well-recognized secretory leader sequence motif, as well as various PCR-based or low stringency hybridization cloning techniques, have advanced the state of the art by making available large numbers of DNA/amino acid sequences for proteins that are known to have biological activity by virtue of their secreted nature in the case of leader sequence cloning, or by virtue of the cell or tissue source in the case of PCR-based techniques. It is to these proteins that the present invention is directed.

SUMMARY OF THE INVENTION

In one embodiment, the present invention provides a composition comprising an isolated protein encoded by a polynucleotide selected from the group consisting of:

(a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:1;

(b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:1 from nucleotide 70 to nucleotide 505;

(c) a polynucleotide comprising the nucleotide sequence of the full length protein coding sequence of clone AP162 deposited under accession number ATCC 98026 ;

(d) a polynucleotide encoding the full length protein encoded by the cDNA insert of clone AP162 deposited under accession number ATCC 98026 ;

(e) a polynucleotide comprising the nucleotide sequence of the mature protein coding sequence of clone AP162 deposited under accession number ATCC 98026 ;

(f) a polynucleotide encoding the mature protein encoded by the cDNA insert of clone AP162 deposited under accession number ATCC 98026 ;

(g) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:2;

(h) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:2 having biological activity;

(i) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(f) above; and

(j) a polynucleotide which encodes a species homologue of the protein of (g) or (h) above.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:1 from nucleotide 70 to nucleotide 505; the nucleotide sequence of the full length protein coding sequence of clone AP162 deposited under accession number ATCC 98026 ; or the nucleotide sequence of the mature protein coding sequence of clone AP162 deposited under accession number ATCC 98026 . In other preferred embodiments, the polynucleotide encodes the full length or mature protein encoded by the cDNA insert of clone AP162 deposited under accession number ATCC 98026 . In yet other preferred embodiments, such polynucleotide encodes a protein comprising the amino acid sequence of SEQ ID NO:2 from amino acid 42 to amino acid 61.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence of SEQ ID NO:2;

(b) the amino acid sequence of SEQ ID NO:2 from amino acid 42 to amino acid 61;

(c) fragments of the amino acid sequence of SEQ ID NO:2; and

(d) the amino acid sequence encoded by the cDNA insert of clone AP162 deposited under accession number ATCC 98026;

the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:2 or the amino acid sequence of SEQ ID NO:2 from amino acid 42 to amino acid 61.

In one embodiment, the present invention provides a composition comprising an isolated protein encoded by a polynucleotide selected from the group consisting of:

(a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:4;

(b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:4 from nucleotide 230 to nucleotide 791;

(c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:4 from nucleotide 311 to nucleotide 791;

(d) a polynucleotide comprising the nucleotide sequence of the full length protein coding sequence of clone AM931 deposited under accession number ATCC 98026 ;

(e) a polynucleotide encoding the full length protein encoded by the cDNA insert of clone AM931 deposited under accession number ATCC 98026 ;

(f) a polynucleotide comprising the nucleotide sequence of the mature protein coding sequence of clone AM931 deposited under accession number ATCC 98026 ;

(g) a polynucleotide encoding the mature protein encoded by the cDNA insert of clone AM931 deposited under accession number ATCC 98026 ;

(h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:5;

(i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:5 having biological activity;

(j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above; and

(k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:4 from nucleotide 230 to nucleotide 791; the nucleotide sequence of SEQ ID NO:4 from nucleotide 311 to nucleotide 791; the nucleotide sequence of the full length protein coding sequence of clone AM931 deposited under accession number ATCC 98026 ; or the

nucleotide sequence of the mature protein coding sequence of clone AM931 deposited under accession number ATCC 98026 . In other preferred embodiments, the polynucleotide encodes the full length or mature protein encoded by the cDNA insert of clone AM931 deposited under accession number ATCC 98026 . In yet other preferred embodiments, such polynucleotide encodes a protein comprising the amino acid sequence of SEQ ID NO:5 from amino acid 32 to amino acid 51.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence of SEQ ID NO:5;

(b) the amino acid sequence of SEQ ID NO:5 from amino acid 32 to amino acid 51;

(c) fragments of the amino acid sequence of SEQ ID NO:5; and

(d) the amino acid sequence encoded by the cDNA insert of clone AM931 deposited under accession number ATCC 98026;

the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:5 or the amino acid sequence of SEQ ID NO:5 from amino acid 32 to amino acid 51.

In one embodiment, the present invention provides a composition comprising an isolated protein encoded by a polynucleotide selected from the group consisting of:

(a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:6;

(b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:6 from nucleotide 14 to nucleotide 491;

(c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:6 from nucleotide 83 to nucleotide 491;

(d) a polynucleotide comprising the nucleotide sequence of the full length protein coding sequence of clone AM610 deposited under accession number ATCC 98026 ;

(e) a polynucleotide encoding the full length protein encoded by the cDNA insert of clone AM610 deposited under accession number ATCC 98026 ;

(f) a polynucleotide comprising the nucleotide sequence of the mature protein coding sequence of clone AM610 deposited under accession number ATCC 98026 ;

(g) a p lynucleotideencoding the mature protein encoded by the cDNA insert of clone AM610 deposited under accession number ATCC 98026 ;

(h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:7;

(i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:7 having biological activity;

(j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above; and

(k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:6 from nucleotide 14 to nucleotide 491; the nucleotide sequence of SEQ ID NO:6 from nucleotide 83 to nucleotide 491; the nucleotide sequence of the full length protein coding sequence of clone AM610 deposited under accession number ATCC 98026 ; or the nucleotide sequence of the mature protein coding sequence of clone AM610 deposited under accession number ATCC 98026 . In other preferred embodiments, the polynucleotide encodes the full length or mature protein encoded by the cDNA insert of clone AM610 deposited under accession number ATCC 98026 . In yet other preferred embodiments, such polynucleotide encodes a protein comprising the amino acid sequence of SEQ ID NO:7 from amino acid 31 to amino acid 50.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence of SEQ ID NO:7;

(b) the amino acid sequence of SEQ ID NO:7 from amino acid 31 to amino acid 50;

(c) fragments of the amino acid sequence of SEQ ID NO:7; and

(d) the amino acid sequence encoded by the cDNA insert of clone AM610 deposited under accession number ATCC 98026;

the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:7 or the amino acid sequence of SEQ ID NO:7 from amino acid 31 to amino acid 50.

In one embodiment, the present invention provides a composition comprising an isolated protein encoded by a polynucleotide selected from the group consisting of:

(a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:9;

(b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:9 from nucleotide 1 to nucleotide 483;

(c) a polynucleotide comprising the nucleotide sequence of the full length protein coding sequence of clone AM340 deposited under accession number ATCC 98026 ;

(d) a polynucleotide encoding the full length protein encoded by the cDNA insert of clone AM340 deposited under accession number ATCC 98026 ;

(e) a polynucleotide comprising the nucleotide sequence of the mature protein coding sequence of clone AM340 deposited under accession number ATCC 98026 ;

(f) a polynucleotide encoding the mature protein encoded by the cDNA insert of clone AM340 deposited under accession number ATCC 98026 ;

(g) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:10;

(h) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:10 having biological activity;

(i) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(f) above; and

(j) a polynucleotide which encodes a species homologue of the protein of (g) or (h) above.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:9 from nucleotide 1 to nucleotide 483; the nucleotide sequence of the full length protein coding sequence of clone AM340 deposited under accession number ATCC 98026 ; or the nucleotide sequence of the mature protein coding sequence of clone AM340 deposited under accession number ATCC 98026 . In other preferred embodiments, the polynucleotide encodes the full length or mature protein encoded by the cDNA insert of clone AM340 deposited under accession number ATCC 98026 . In yet other preferred embodiments, such polynucleotide encodes a protein comprising the amino acid sequence of SEQ ID NO:10 from amino acid 124 to amino acid 143.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence of SEQ ID NO:10;

(b) the amino acid sequence of SEQ ID NO:10 from amino acid 124 to amino acid 143;

(c) fragments of the amino acid sequence of SEQ ID NO:10; and

(d) the amino acid sequence encoded by the cDNA insert of clone AM340 deposited under accession number ATCC 98026;

the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:10 or the amino acid sequence of SEQ ID NO:10 from amino acid 124 to amino acid 143.

In one embodiment, the present invention provides a composition comprising an isolated protein encoded by a polynucleotide selected from the group consisting of:

(a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:11;

(b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:11 from nucleotide 15 to nucleotide 462;

(c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:11 from nucleotide 87 to nucleotide 462;

(d) a polynucleotide comprising the nucleotide sequence of the full length protein coding sequence of clone AM282 deposited under accession number ATCC 98026 ;

(e) a polynucleotide encoding the full length protein encoded by the cDNA insert of clone AM282 deposited under accession number ATCC 98026 ;

(f) a polynucleotide comprising the nucleotide sequence of the mature protein coding sequence of clone AM282 deposited under accession number ATCC 98026 ;

(g) a polynucleotide encoding the mature protein encoded by the cDNA insert of clone AM282 deposited under accession number ATCC 98026 ;

(h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:12;

(i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:12 having biological activity;

(j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above; and

(k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:11 from nucleotide 15 to nucleotide 462; the nucleotide sequence of SEQ ID NO:11 from nucleotide 87 to nucleotide 462; the nucleotide sequence of the full length protein coding sequence of clone AM282 deposited under accession number ATCC 98026 ; or the nucleotide sequence of the mature protein coding sequence of clone AM282 deposited under accession number ATCC 98026 . In other preferred embodiments, the polynucleotide encodes the full length or mature protein encoded by the cDNA insert of clone AM282 deposited under accession number ATCC 98026 . In yet other preferred embodiments, such polynucleotide encodes a protein comprising the amino acid sequence of SEQ ID NO:12 from amino acid 28 to amino acid 47.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence of SEQ ID NO:12;

(b) the amino acid sequence of SEQ ID NO:12 from amino acid 28 to amino acid 47;

(c) fragments of the amino acid sequence of SEQ ID NO:12; and

(d) the amino acid sequence encoded by the cDNA insert of clone AM282 deposited under accession number ATCC 98026;

the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:12 or the amino acid sequence of SEQ ID NO:12 from amino acid 28 to amino acid 47.

In one embodiment, the present invention provides a composition comprising an isolated protein encoded by a polynucleotide selected from the group consisting of:

(a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:14;

(b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:14 from nucleotide 185 to nucleotide 519;

(c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:14 from nucleotide 260 to nucleotide 519;

(d) a polynucleotide comprising the nucleotide sequence of the full length protein c ding sequence of clone AK647 deposited under accession number ATCC 98026 ;

(e) a polynucleotide encoding the full length protein encoded by the cDNA insert of clone AK647 deposited under accession number ATCC 98026 ;

(f) a polynucleotide comprising the nucleotide sequence of the mature protein coding sequence of clone AK647 deposited under accession number ATCC 98026 ;

(g) a polynucleotide encoding the mature protein encoded by the cDNA insert of clone AK647 deposited under accession number ATCC 98026 ;

(h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:15;

(i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:15 having biological activity;

(j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above; and

(k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:14 from nucleotide 185 to nucleotide 519; the nucleotide sequence of SEQ ID NO:14 from nucleotide 260 to nucleotide 519; the nucleotide sequence of the full length protein coding sequence of clone AK647 deposited under accession number ATCC 98026 ; or the nucleotide sequence of the mature protein coding sequence of clone AK647 deposited under accession number ATCC 98026 . In other preferred embodiments, the polynucleotide encodes the full length or mature protein encoded by the cDNA insert of clone AK647 deposited under accession number ATCC 98026 . In yet other preferred embodiments, such polynucleotide encodes a protein comprising the amino acid sequence of SEQ ID NO:15 from amino acid 27 to amino acid 46.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence of SEQ ID NO:15;

(b) the amino acid sequence of SEQ ID NO:15 from amino acid 27 to amino acid 46;

(c) fragments of the amin acid sequence of SEQ ID NO:15; and

(d) the amino acid sequence encoded by the cDNA insert of clone AK647 deposited under accession number ATCC 98026;

the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:15 or the amino acid sequence of SEQ ID NO:15 from amino acid 27 to amino acid 46.

In one embodiment, the present invention provides a composition comprising an isolated protein encoded by a polynucleotide selected from the group consisting of:

(a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:17;

(b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:17 from nucleotide 257 to nucleotide 536;

(c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:17 from nucleotide 329 to nucleotide 536;

(d) a polynucleotide comprising the nucleotide sequence of the full length protein coding sequence of clone AK583 deposited under accession number ATCC 98026 ;

(e) a polynucleotide encoding the full length protein encoded by the cDNA insert of clone AK583 deposited under accession number ATCC 98026 ;

(f) a polynucleotide comprising the nucleotide sequence of the mature protein coding sequence of clone AK583 deposited under accession number ATCC 98026 ;

(g) a polynucleotide encoding the mature protein encoded by the cDNA insert of clone AK583 deposited under accession number ATCC 98026 ;

(h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:18;

(i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:18 having biological activity;

(j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above; and

(k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:17 from nucleotide 257 to nucleotide 536; the nucleotide sequence of SEQ ID NO:17

from nucleotide 329 to nucleotide 536; the nucleotide sequence of the full length protein coding sequence of clone AK583 deposited under accession number ATCC 98026 ; or the nucleotide sequence of the mature protein coding sequence of clone AK583 deposited under accession number ATCC 98026 . In other preferred embodiments, the polynucleotide encodes the full length or mature protein encoded by the cDNA insert of clone AK583 deposited under accession number ATCC 98026 . In yet other preferred embodiments, such polynucleotide encodes a protein comprising the amino acid sequence of SEQ ID NO:18 from amino acid 14 to amino acid 33.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence of SEQ ID NO:18;

(b) the amino acid sequence of SEQ ID NO:18 from amino acid 14 to amino acid 33;

(c) fragments of the amino acid sequence of SEQ ID NO:18; and

(d) the amino acid sequence encoded by the cDNA insert of clone AK583 deposited under accession number ATCC 98026;

the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:18 or the amino acid sequence of SEQ ID NO:18 from amino acid 14 to amino acid 33.

In one embodiment, the present invention provides a composition comprising an isolated protein encoded by a polynucleotide selected from the group consisting of:

(a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:20;

(b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:20 from nucleotide 179 to nucleotide 476;

(c) a polynucleotide comprising the nucleotide sequence of the full length protein coding sequence of clone AK533 deposited under accession number ATCC 98026 ;

(d) a polynucleotide encoding the full length protein encoded by the cDNA insert of clone AK533 deposited under accession number ATCC 98026 ;

(e) a polynucleotide comprising the nucleotide sequence of the mature protein coding sequence of clone AK533 deposited under accession number ATCC 98026 ;

(f) a polynucleotide encoding the mature protein encoded by the cDNA insert of clone AK533 deposited under accession number ATCC 98026 ;

(g) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:21;

(h) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:21 having biological activity;

(i) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(f) above; and

(j) a polynucleotide which encodes a species homologue of the protein of (g) or (h) above.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:20 from nucleotide 179 to nucleotide 476; the nucleotide sequence of the full length protein coding sequence of clone AK533 deposited under accession number ATCC 98026 ; or the nucleotide sequence of the mature protein coding sequence of clone AK533 deposited under accession number ATCC 98026 . In other preferred embodiments, the polynucleotide encodes the full length or mature protein encoded by the cDNA insert of clone AK533 deposited under accession number ATCC 98026 . In yet other preferred embodiments, such polynucleotide encodes a protein comprising the amino acid sequence of SEQ ID NO:21 from amino acid 35 to amino acid 57.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence of SEQ ID NO:21;

(b) the amino acid sequence of SEQ ID NO:21 from amino acid 35 to amino acid 57;

(c) fragments of the amino acid sequence of SEQ ID NO:21; and

(d) the amino acid sequence encoded by the cDNA insert of clone AK533 deposited under accession number ATCC 98026;

the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:21 or the amino acid sequence of SEQ ID NO:21 from amino acid 35 to amino acid 57.

In one embodiment, the present invention provides a composition comprising an isolated protein encoded by a polynucleotide selected from the group consisting of:

(a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:23;

(b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:23 from nucleotide 220 to nucleotide 612;

(c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:23 from nucleotide 328 to nucleotide 612;

(d) a polynucleotide comprising the nucleotide sequence of the full length protein coding sequence of clone AK296 deposited under accession number ATCC 98026 ;

(e) a polynucleotide encoding the full length protein encoded by the cDNA insert of clone AK296 deposited under accession number ATCC 98026 ;

(f) a polynucleotide comprising the nucleotide sequence of the mature protein coding sequence of clone AK296 deposited under accession number ATCC 98026 ;

(g) a polynucleotideencoding the mature protein encoded by the cDNA insert of clone AK296 deposited under accession number ATCC 98026 ;

(h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:24;

(i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:24 having biological activity;

(j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above; and

(k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:23 from nucleotide 220 to nucleotide 612; the nucleotide sequence of SEQ ID NO:23 from nucleotide 328 to nucleotide 612; the nucleotide sequence of the full length protein coding sequence of clone AK296 deposited under accession number ATCC 98026 ; or the nucleotide sequence of the mature protein coding sequence of clone AK296 deposited under accession number ATCC 98026 . In other preferred embodiments, the polynucleotide encodes the full length or mature protein encoded by the cDNA insert of clone AK296 deposited under accession number ATCC 98026 . In yet other preferred embodiments, such polynucleotide encodes a protein comprising the amino acid sequence of SEQ ID NO:24 from amino acid 81 to amino acid 90.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence of SEQ ID NO:24;

(b) the amino acid sequence of SEQ ID NO:24 from amino acid 81 to amino acid 90;

(c) fragments of the amino acid sequence of SEQ ID NO:24; and

(d) the amino acid sequence encoded by the cDNA insert of clone AK296 deposited under accession number ATCC 98026;

the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:24 or the amino acid sequence of SEQ ID NO:24 from amino acid 81 to amino acid 90.

In one embodiment, the present invention provides a composition comprising an isolated protein encoded by a polynucleotide selected from the group consisting of:

(a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:26;

(b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:26 from nucleotide 58 to nucleotide 655;

(c) a polynucleotide comprising the nucleotide sequence of the full length protein coding sequence of clone H617 deposited under accession number ATCC 98026 ;

(d) a polynucleotide encoding the full length protein encoded by the cDNA insert of clone H617 deposited under accession number ATCC 98026 ;

(e) a polynucleotide comprising the nucleotide sequence of the mature protein coding sequence of clone H617 deposited under accession number ATCC 98026 ;

(f) a polynucleotideencoding the mature protein encoded by the cDNA insert of clone H617 deposited under accession number ATCC 98026 ;

(g) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:27;

(h) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:27 having biological activity;

(i) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(f) above; and

(j) a polynucleotide which encodes a species homologue of the protein of (g) or (h) above.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:26 from nucleotide 58 to nucleotide 655; the nucleotide sequence of the full length protein coding sequence of clone H617 deposited under accession number ATCC 98026 ; or the nucleotide sequence of the mature protein coding sequence of clone H617 deposited under accession number ATCC 98026 . In other preferred embodiments, the polynucleotide encodes the full length or mature protein encoded by the cDNA insert of clone H617 deposited under accession number ATCC 98026 . In yet other preferred embodiments, such polynucleotide encodes a protein comprising the amino acid sequence of SEQ ID NO:27 from amino acid 65 to amino acid 84.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence of SEQ ID NO:27;

(b) the amino acid sequence of SEQ ID NO:27 from amino acid 65 to amino acid 84;

(c) fragments of the amino acid sequence of SEQ ID NO:27; and

(d) the amino acid sequence encoded by the cDNA insert of clone H617 deposited under accession number ATCC 98026;

the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:27 or the amino acid sequence of SEQ ID NO:27 from amino acid 65 to amino acid 84.

In one embodiment, the present invention provides a composition comprising an isolated protein encoded by a polynucleotide selected from the group consisting of:

(a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:29;

(b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:29 from nucleotide 14 to nucleotide 391;

(c) a polynucleotide comprising the nucleotide sequence of the full length protein coding sequence of clone BB9 deposited under accession number ATCC 98026 ;

(d) a polynucleotide encoding the full length protein encoded by the cDNA insert of clone BB9 deposited under accession number ATCC 98026 ;

(e) a polynucleotide comprising the nucleotide sequence of the mature protein coding sequence of clone BB9 deposited under accession number ATCC 98026 ;

(f) a polynucleotide encoding the mature protein encoded by the cDNA insert of clone BB9 deposited under accession number ATCC 98026 ;

(g) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:30;

(h) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:30 having biological activity;

(i) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(f) above; and

(j) a polynucleotide which encodes a species homologue of the protein of (g) or (h) above.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:29 from nucleotide 14 to nucleotide 391; the nucleotide sequence of the full length protein coding sequence of clone BB9 deposited under accession number ATCC 98026 ; or the nucleotide sequence of the mature protein coding sequence of clone BB9 deposited under accession number ATCC 98026 . In other preferred embodiments, the polynucleotide encodes the full length or mature protein encoded by the cDNA insert of clone BB9 deposited under accession number ATCC 98026 . In yet other preferred embodiments, such polynucleotide encodes a protein comprising the amino acid sequence of SEQ ID NO:30 from amino acid 75 to amino acid 94.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence of SEQ ID NO:30;

(b) the amino acid sequence of SEQ ID NO:30 from amino acid 75 to amino acid 94;

(c) fragments of the amino acid sequence of SEQ ID NO:30; and

(d) the amino acid sequence encoded by the cDNA insert of clone BB9 deposited under accession number ATCC 98026;

the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:30 or the amino acid sequence of SEQ ID NO:30 from amino acid 75 to amino acid 94.

In ne embodiment, the present invention provides a composition comprising an isolated protein encoded by a polynucleotide selected from the group consisting of:

(a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:32;

(b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:32 from nucleotide 61 to nucleotide 514;

(c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:32 from nucleotide 115 to nucleotide 514;

(d) a polynucleotide comprising the nucleotide sequence of the full length protein coding sequence of clone AW191 deposited under accession number ATCC 98026 ;

(e) a polynucleotide encoding the full length protein encoded by the cDNA insert of clone AW191 deposited under accession number ATCC 98026 ;

(f) a polynucleotide comprising the nucleotide sequence of the mature protein coding sequence of clone AW191 deposited under accession number ATCC 98026 ;

(g) a polynucleotide encoding the mature protein encoded by the cDNA insert of clone AW191 deposited under accession number ATCC 98026 ;

(h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:33;

(i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:33 having biological activity;

(j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above; and

(k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:32 from nucleotide 61 to nucleotide 514; the nucleotide sequence of SEQ ID NO:32 from nucleotide 115 to nucleotide 514; the nucleotide sequence of the full length protein coding sequence of clone AW191 deposited under accession number ATCC 98026 ; or the nucleotide sequence of the mature protein coding sequence of clone AW191 deposited under accession number ATCC 98026 . In other preferred embodiments, the polynucleotide encodes the full length or mature protein encoded by the cDNA insert of clone AW191 deposited under accession number ATCC 98026 . In yet other preferred embodiments,

such polynucleotide encodes a pr tein comprising the amino acid sequence of SEQ ID NO:33 from amino acid 24 to amino acid 43.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence of SEQ ID NO:33;

(b) the amino acid sequence of SEQ ID NO:33 from amino acid 24 to amino acid 43;

(c) fragments of the amino acid sequence of SEQ ID NO:33; and

(d) the amino acid sequence encoded by the cDNA insert of clone AW191 deposited under accession number ATCC 98026;

the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:33 or the amino acid sequence of SEQ ID NO:33 from amino acid 24 to amino acid 43.

In one embodiment, the present invention provides a composition comprising an isolated protein encoded by a polynucleotide selected from the group consisting of:

(a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:35;

(b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:35 from nucleotide 180 to nucleotide 525;

(c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:35 from nucleotide 339 to nucleotide 525;

(d) a polynucleotide comprising the nucleotide sequence of the full length protein coding sequence of clone AT211 deposited under accession number ATCC 98026 ;

(e) a polynucleotide encoding the full length protein encoded by the cDNA insert of clone AT211 deposited under accession number ATCC 98026 ;

(f) a polynucleotide comprising the nucleotide sequence of the mature protein coding sequence of clone AT211 deposited under accession number ATCC 98026 ;

(g) a polynucleotide encoding the mature protein encoded by the cDNA insert of clone AT211 deposited under accession number ATCC 98026 ;

(h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:36;

(i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:36 having biological activity;

(j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above; and

(k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:35 from nucleotide 180 to nucleotide 525; the nucleotide sequence of SEQ ID NO:35 from nucleotide 339 to nucleotide 525; the nucleotide sequence of the full length protein coding sequence of clone AT211 deposited under accession number ATCC 98026 ; or the nucleotide sequence of the mature protein coding sequence of clone AT211 deposited under accession number ATCC 98026 . In other preferred embodiments, the polynucleotide encodes the full length or mature protein encoded by the cDNA insert of clone AT211 deposited under accession number ATCC 98026 . In yet other preferred embodiments, such polynucleotide encodes a protein comprising the amino acid sequence of SEQ ID NO:36 from amino acid 1 to amino acid 20.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence of SEQ ID NO:36;

(b) the amino acid sequence of SEQ ID NO:36 from amino acid 1 to amino acid 20;

(c) fragments of the amino acid sequence of SEQ ID NO:36; and

(d) the amino acid sequence encoded by the cDNA insert of clone AT211 deposited under accession number ATCC 98026;

the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:36 or the amino acid sequence of SEQ ID NO:36 from amino acid 1 to amino acid 20.

In one embodiment, the present invention provides a composition comprising an isolated protein encoded by a polynucleotide selected from the group consisting of:

(a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:38;

(b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:38 from nucleotide 225 to nucleotide 677;

(c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:38 from nucleotide 390 to nucleotide 677;

(d) a polynucleotide comprising the nucleotide sequence of the full length protein coding sequence of clone AT205 deposited under accession number ATCC 98026 ;

(e) a polynucleotide encoding the full length protein encoded by the cDNA insert of clone AT205 deposited under accession number ATCC 98026 ;

(f) a polynucleotide comprising the nucleotide sequence of the mature protein coding sequence of clone AT205 deposited under accession number ATCC 98026 ;

(g) a polynucleotide encoding the mature protein encoded by the cDNA insert of clone AT205 deposited under accession number ATCC 98026 ;

(h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:39;

(i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:39 having biological activity;

(j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above; and

(k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:38 from nucleotide 225 to nucleotide 677; the nucleotide sequence of SEQ ID NO:38 from nucleotide 390 to nucleotide 677; the nucleotide sequence of the full length protein coding sequence of clone AT205 deposited under accession number ATCC 98026 ; or the nucleotide sequence of the mature protein coding sequence of clone AT205 deposited under accession number ATCC 98026 . In other preferred embodiments, the polynucleotide encodes the full length or mature protein encoded by the cDNA insert of clone AT205 deposited under accession number ATCC 98026 . In yet other preferred embodiments, such polynucleotide encodes a protein comprising the amino acid sequence of SEQ ID NO:39 from amino acid 6 to amino acid 25.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence of SEQ ID NO:39;

(b) the amino acid sequence of SEQ ID NO:39 from amino acid 6 to amino acid 25;

(c) fragments of the amino acid sequence of SEQ ID NO:39; and

(d) the amino acid sequence encoded by the cDNA insert of clone AT205 deposited under accession number ATCC 98026;

the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:39 or the amino acid sequence of SEQ ID NO:39 from amino acid 6 to amino acid 25.

In one embodiment, the present invention provides a composition comprising an isolated protein encoded by a polynucleotide selected from the group consisting of:

(a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:40;

(b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:40 from nucleotide 128 to nucleotide 508;

(c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:40 from nucleotide 200 to nucleotide 508;

(d) a polynucleotide comprising the nucleotide sequence of the full length protein coding sequence of clone AS34 deposited under accession number ATCC 98026 ;

(e) a polynucleotide encoding the full length protein encoded by the cDNA insert of clone AS34 deposited under accession number ATCC 98026 ;

(f) a polynucleotide comprising the nucleotide sequence of the mature protein coding sequence of clone AS34 deposited under accession number ATCC 98026 ;

(g) a polynucleotide encoding the mature protein encoded by the cDNA insert of clone AS34 deposited under accession number ATCC 98026 ;

(h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:41;

(i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:41 having biological activity;

(j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above; and

(k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:40 from nucleotide 128 t nucleotide 508; the nucleotide sequence of SEQ ID NO:40 from nucleotide 200 to nucleotide 508; the nucleotide sequence of the full length protein coding sequence of clone AS34 deposited under accession number ATCC 98026 ; or the nucleotide sequence of the mature protein coding sequence of clone AS34 deposited under accession number ATCC 98026 . In other preferred embodiments, the polynucleotide encodes the full length or mature protein encoded by the cDNA insert of clone AS34 deposited under accession number ATCC 98026 . In yet other preferred embodiments, such polynucleotide encodes a protein comprising the amino acid sequence of SEQ ID NO:41 from amino acid 27 to amino acid 46.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence of SEQ ID NO:41;

(b) the amino acid sequence of SEQ ID NO:41 from amino acid 27 to amino acid 46;

(c) fragments of the amino acid sequence of SEQ ID NO:41; and

(d) the amino acid sequence encoded by the cDNA insert of clone AS34 deposited under accession number ATCC 98026;

the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:41 or the amino acid sequence of SEQ ID NO:41 from amino acid 27 to amino acid 46.

In one embodiment, the present invention provides a composition comprising an isolated protein encoded by a polynucleotide selected from the group consisting of:

(a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:43;

(b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:43 from nucleotide 23 to nucleotide 676;

(c) a polynucleotide comprising the nucleotide sequence of the full length protein coding sequence of clone AS32 deposited under accession number ATCC 98026 ;

(d) a polynucleotide encoding the full length protein encoded by the cDNA insert of clone AS32 deposited under accession number ATCC 98026 ;

(e) a polynucleotide comprising the nucleotide sequence f the mature protein coding sequence of clone AS32 deposited under accessi n number ATCC 98026 ;

(f) a polynucleotide encoding the mature protein encoded by the cDNA insert of clone AS32 deposited under accession number ATCC 98026 ;

(g) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:44;

(h) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:44 having biological activity;

(i) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(f) above; and

(j) a polynucleotide which encodes a species homologue of the protein of (g) or (h) above.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:43 from nucleotide 23 to nucleotide 676; the nucleotide sequence of the full length protein coding sequence of clone AS32 deposited under accession number ATCC 98026 ; or the nucleotide sequence of the mature protein coding sequence of clone AS32 deposited under accession number ATCC 98026 . In other preferred embodiments, the polynucleotide encodes the full length or mature protein encoded by the cDNA insert of clone AS32 deposited under accession number ATCC 98026 . In yet other preferred embodiments, such polynucleotide encodes a protein comprising the amino acid sequence of SEQ ID NO:44 from amino acid 78 to amino acid 97.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence of SEQ ID NO:44;

(b) the amino acid sequence of SEQ ID NO:44 from amino acid 78 to amino acid 97;

(c) fragments of the amino acid sequence of SEQ ID NO:44; and

(d) the amino acid sequence encoded by the cDNA insert of clone AS32 deposited under accession number ATCC 98026;

the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:44 or the amino acid sequence of SEQ ID NO:44 from amino acid 78 to amino acid 97.

In one embodiment, the present invention provides a composition comprising an isolated protein encoded by a polynucleotide selected from the group consisting of:

(a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:46;

(b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:46 from nucleotide 132 to nucleotide 479;

(c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:46 from nucleotide 201 to nucleotide 479;

(d) a polynucleotide comprising the nucleotide sequence of the full length protein coding sequence of clone AR260 deposited under accession number ATCC 98026 ;

(e) a polynucleotide encoding the full length protein encoded by the cDNA insert of clone AR260 deposited under accession number ATCC 98026 ;

(f) a polynucleotide comprising the nucleotide sequence of the mature protein coding sequence of clone AR260 deposited under accession number ATCC 98026 ;

(g) a polynucleotide encoding the mature protein encoded by the cDNA insert of clone AR260 deposited under accession number ATCC 98026 ;

(h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:47;

(i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:47 having biological activity;

(j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above; and

(k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:46 from nucleotide 132 to nucleotide 479; the nucleotide sequence of SEQ ID NO:46 from nucleotide 201 to nucleotide 479; the nucleotide sequence of the full length protein coding sequence of clone AR260 deposited under accession number ATCC 98026 ; or the nucleotide sequence of the mature protein coding sequence of clone AR260 deposited under accession number ATCC 98026 . In other preferred embodiments, the polynucleotide encodes the full length or mature protein encoded by the cDNA insert of clone AR260 deposited under accession number ATCC 98026 . In yet other preferred embodiments,

such polynucleotide encodes a protein comprising the amino acid sequence of SEQ ID NO:47 from amino acid 40 to amino acid 59.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence of SEQ ID NO:47;

(b) the amino acid sequence of SEQ ID NO:47 from amino acid 40 to amino acid 59;

(c) fragments of the amino acid sequence of SEQ ID NO:47; and

(d) the amino acid sequence encoded by the cDNA insert of clone AR260 deposited under accession number ATCC 98026;

the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:47 or the amino acid sequence of SEQ ID NO:47 from amino acid 40 to amino acid 59.

In one embodiment, the present invention provides a composition comprising an isolated protein encoded by a polynucleotide selected from the group consisting of:

(a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:50;

(b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:50 from nucleotide 1 to nucleotide 332;

(c) a polynucleotide comprising the nucleotide sequence of the full length protein coding sequence of clone K640 deposited under accession number ATCC 98026 ;

(d) a polynucleotide encoding the full length protein encoded by the cDNA insert of clone K640 deposited under accession number ATCC 98026 ;

(e) a polynucleotide comprising the nucleotide sequence of the mature protein coding sequence of clone K640 deposited under accession number ATCC 98026 ;

(f) a polynucleotide encoding the mature protein encoded by the cDNA insert of clone K640 deposited under accession number ATCC 98026 ;

(g) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:51;

(h) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:51 having biological activity;

(i) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(f) above; and

(j) a polynucleotide which encodes a species homologue of the protein of (g) or (h) above.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:50 from nucleotide 1 to nucleotide 332; the nucleotide sequence of the full length protein coding sequence of clone K640 deposited under accession number ATCC 98026 ; or the nucleotide sequence of the mature protein coding sequence of clone K640 deposited under accession number ATCC 98026 . In other preferred embodiments, the polynucleotide encodes the full length or mature protein encoded by the cDNA insert of clone K640 deposited under accession number ATCC 98026 . In yet other preferred embodiments such polynucleotide encodes a protein comprising the amino acid sequence of SEQ ID NO:51 from amino acid 11 to amino acid 30.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence of SEQ ID NO:51;

(b) the amino acid sequence of SEQ ID NO:51 from amino acid 11 to amino acid 30;

(c) fragments of the amino acid sequence of SEQ ID NO:51; and

(d) the amino acid sequence encoded by the cDNA insert of clone K640 deposited under accession number ATCC 98026;

the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:51 or the amino acid sequence of SEQ ID NO:51 from amino acid 11 to amino acid 30.

In one embodiment, the present invention provides a composition comprising an isolated protein encoded by a polynucleotide selected from the group consisting of:

(a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:54;

(b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:54 from nucleotide 71 to nucleotide 377;

(c) a polynucleotide comprising the nucleotide sequence of the full length protein coding sequence of clone K39 deposited under accession number ATCC 98026 ;

(d) a polynucleotide encoding the full length protein encoded by the cDNA insert of cl ne K39 deposited under accession number ATCC 98026 ;

(e) a polynucleotide comprising the nucleotide sequence of the mature protein coding sequence of clone K39 deposited under accession number ATCC 98026 ;

(f) a polynucleotide encoding the mature protein encoded by the cDNA insert of clone K39 deposited under accession number ATCC 98026 ;

(g) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:55;

(h) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:55 having biological activity;

(i) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(f) above; and

(j) a polynucleotide which encodes a species homologue of the protein of (g) or (h) above.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:54 from nucleotide 71 to nucleotide 377; the nucleotide sequence of the full length protein coding sequence of clone K39 deposited under accession number ATCC 98026 ; or the nucleotide sequence of the mature protein coding sequence of clone K39 deposited under accession number ATCC 98026 . In other preferred embodiments, the polynucleotide encodes the full length or mature protein encoded by the cDNA insert of clone K39 deposited under accession number ATCC 98026 . In yet other preferred embodiments, such polynucleotide encodes a protein comprising the amino acid sequence of SEQ ID NO:55 from amino acid 62 to amino acid 81.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence of SEQ ID NO:55;

(b) the amino acid sequence of SEQ ID NO:55 from amino acid 62 to amino acid 81;

(c) fragments of the amino acid sequence of SEQ ID NO:55; and

(d) the amino acid sequence encoded by the cDNA insert of clone K39 deposited under accession number ATCC 98026;

the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:55 or the amino acid sequence of SEQ ID NO:55 from amino acid 62 to amino acid 81.

In one embodiment, the present invention provides a composition comprising an isolated protein encoded by a polynucleotide selected from the group consisting of:

(a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:57;

(b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:57 from nucleotide 194 to nucleotide 423;

(c) a polynucleotide comprising the nucleotide sequence of the full length protein coding sequence of clone AT319 deposited under accession number ATCC 98026 ;

(d) a polynucleotide encoding the full length protein encoded by the cDNA insert of clone AT319 deposited under accession number ATCC 98026 ;

(e) a polynucleotide comprising the nucleotide sequence of the mature protein coding sequence of clone AT319 deposited under accession number ATCC 98026 ;

(f) a polynucleotide encoding the mature protein encoded by the cDNA insert of clone AT319 deposited under accession number ATCC 98026 ;

(g) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:58;

(h) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:58 having biological activity;

(i) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(f) above; and

(j) a polynucleotide which encodes a species homologue of the protein of (g) or (h) above.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:57 from nucleotide 194 to nucleotide 423; the nucleotide sequence of the full length protein coding sequence of clone AT319 deposited under accession number ATCC 98026 ; or the nucleotide sequence of the mature protein coding sequence of clone AT319 deposited under accession number ATCC 98026 . In other preferred embodiments, the polynucleotide encodes the full length or mature protein encoded by the cDNA insert of clone AT319 deposited under accession number ATCC 98026 . In yet other preferred

embodiments, such polynucleotide encodes a protein comprising the amino acid sequence of SEQ ID NO:58 from amino acid 2 to amino acid 21.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence of SEQ ID NO:58;

(b) the amino acid sequence of SEQ ID NO:58 from amino acid 2 to amino acid 21;

(c) fragments of the amino acid sequence of SEQ ID NO:58; and

(d) the amino acid sequence encoded by the cDNA insert of clone AT319 deposited under accession number ATCC 98026;

the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:58 or the amino acid sequence of SEQ ID NO:58 from amino acid 2 to amino acid 21.

Protein compositions of the present invention may further comprise a pharmaceutically acceptable carrier. Compositions comprising an antibody which specifically reacts with such protein are also provided by the present invention.

Methods are also provided for preventing, treating or ameliorating a medical condition which comprises administering to a mammalian subject a therapeutically effective amount of a composition comprising a protein of the present invention and a pharmaceutically acceptable carrier.

BRIEF DESCRIPTION OF THE FIGURES

Fig. 1 is an autoradiograph evidencing the expression of clones AP162, AM931, and AR260 in COS cells (expressed band(s) indicated by dot(s)).

Fig. 2 is an autoradiograph evidencing the expression of clone AM610 in COS cells (expressed band(s) indicated by dot(s)).

Fig. 3 is an autoradiograph evidencing the expression of clones AM340, AM282 and AK533 in COS cells (expressed band(s) indicated by dot(s)).

Fig. 4 is an aut radiograph evidencing the expression of clone AK647 in COS cells (expressed band(s) indicated by dot(s)).

Fig. 5 is an autoradiograph evidencing the expression of clones AH583, AK296, and AS32 in COS cells (expressed band(s) indicated by dot(s)).

Fig. 6 is an autoradiograph evidencing the expression of clones H617 and AT205 in COS cells (expressed band(s) indicated by dot(s)).

Fig. 7 is an autoradiograph evidencing the expression of clones BB9 and K39 in COS cells (expressed band(s) indicated by dot(s)).

Fig. 8 is an autoradiograph evidencing the expression of clones AW191 and AS34 in COS cells (expressed band(s) indicated by dot(s)).

Fig. 9 is an autoradiograph evidencing the expression of clones AT211 and AT319 in COS cells (expressed band(s) indicated by dot(s)).

Fig. 10 is an autoradiograph evidencing the expression of clone K640 in COS cells (expressed band(s) indicated by dot(s)).

DETAILED DESCRIPTION

ISOLATED PROTEINS

Nucleotide and amino acid sequences are reported below for each clone and protein disclosed in the present application. In some instances the sequences are preliminary and may include some incorrect or ambiguous bases or amino acids. The actual nucleotide sequence of each clone can readily be determined by sequencing of the deposited clone in accordance with known methods. The predicted amino acid sequence (both full length and mature) can then be determined from such nucleotide sequence. The amino acid sequence of the protein encoded by a particular clone can also be determined by expression of the clone in a suitable host cell, collecting the protein and determining its sequence.

For each disclosed protein applicants have identified what they have determined to be the reading frame best identifiable with sequence information available at the time of filing. Because of the partial ambiguity in reported sequence information, reported protein sequences include "Xaa" designators. These "Xaa" designators indicate either (1) a residue which cannot be identified because of nucleotide sequence ambiguity or (2) a stop codon in the determined nucleotide sequence where applicants believe one should not exist (if the nucleotide sequence were determined definitively).

As used herein a "secreted" protein is one which, when expressed in a suitable host cell, is transported across or through a membrane, including transport as a result of signal sequences in its amino acid sequence. "Secreted" proteins include without limitation proteins secreted wholly (e.g., soluble proteins) or partially (e.g. , receptors) from the cell in which they are expressed. "Secreted" proteins also include without limitation proteins which are transported across the membrane of the endoplpasmic reticulum.

Protein "AP162"

One protein of the present invention has been identified as protein "AP162". A partial cDNA clone encoding AP162 was first isolated from a human adult placenta cDNA library using methods which are selective for cDNAs encoding secreted proteins. The nucleotide sequence of such partial cDNA was determined and searched against the GenBank database using BLASTA/BLASTX and FASTA search protocols. The search revealed at least some identity with an EST reported by the I.M.A.G.E. Consortium identified as "yu40d08.r1 Homo sapiens cDNA clone 23671 5'" (GenBank accession number H62096). The search also found a hit at GenBank accession number H98192. The human cDNA clone corresponding to the EST database entry was ordered from Genome Systems, Inc., St. Louis, Mo, a distributor of the I.M.A.G.E. Consortium library. The clone received from the distributor was examined and determined to be a full length clone, including a 5' end and 3' UTR (including a polyA tail). This full-length clone is also referred to herein as "AP162".

Applicants' methods identified clone AP162 as encoding a secreted protein.

The nucleotide sequence of the 5' portion of AP162 as presently determined is reported in SEQ ID NO:1. What applicants believe is the proper reading frame and the predicted N-terminal amino acid sequence of the full length AP162 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:2. Additional nucleotide sequence from the 3' portion of AP162, including the polyA tail, is reported in SEQ ID NO:3.

Protein "AM931"

One protein of the present invention has been identified as protein "AM931". A partial cDNA clone encoding AM931 was first isolated from a human fetal kidney cDNA library using methods which are selective for cDNAs encoding secreted proteins. The nucleotide sequence of such partial cDNA was determined and searched against the GenBank database using BLASTA/BLASTX and FASTA search protocols. The search revealed at least some identity with an EST reported by the I.M.A.G.E. Consortium identified as "yh63e02.r1 Homo sapeins cDNA clone 134426 5'" (GenBank accession number R32076). The search also found a hit at GenBank accession number N30331. The human cDNA clone corresponding to the EST database entry was ordered from Genome Systems, Inc., St. Louis, Mo, a distributor of the I.M.A.G.E. Consortium library. The clone received from the distributor was examined and determined to be a full length clone, including a 5' end and 3' UTR (including a polyA tail). This full-length clone is also referred to herein as "AM931".

Applicants' methods identified clone AM931 as encoding a secreted protein.

The nucleotide sequence of AM931 as presently determined is reported in SEQ ID NO:4. What applicants believe is the proper reading frame and the predicted amino acid sequence of the full length AM931 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:5. Amino acids 1 to 27 are the predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 28.

Protein "AM610"

One protein of the present invention has been identified as protein "AM610". A partial cDNA clone encoding AM610 was first isolated from a human fetal kidney cDNA library using methods which are selective for cDNAs encoding secreted proteins. The nucleotide sequence of such partial cDNA was determined and searched against the GenBank database using BLASTA/BLASTX and FASTA search protocols. The search revealed at least some identity with an EST reported by the I.M.A.G.E. Consortium identified as "ym01a10.r1 Human EST 46249 5'" (GenBank accession number H09925). The search also found hits at GenBank accession numbers H09926 and R14298. The human cDNA clone corresponding to the EST database entry was ordered from Genome Systems, Inc., St. Louis, Mo, a distributor of the I.M.A.G.E. Consortium library. The clone received from the distributor was examined and determined to be a full length clone,

including a 5' end and 3' UTR (including a polyA tail). This full-length clone is also referred to herein as "AM610".

Applicants' methods identified clone AM610 as encoding a secreted protein.

The nucleotide sequence of the 5' portion of AM610 as presently determined is reported in SEQ ID NO:6. What applicants believe is the proper reading frame and the predicted N-terminal amino acid sequence of the full length AM610 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:7. Amino acids 1 to 23 are the predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 24. Additional nucleotide sequence from the 3' portion of AM610, including the polyA tail, is reported in SEQ ID NO:8.

Protein "AM340"

One protein of the present invention has been identified as protein "AM340". A partial cDNA clone encoding AM340 was first isolated from a human fetal kidney cDNA library using methods which are selective for cDNAs encoding secreted proteins. The nucleotide sequence of such partial cDNA was determined and searched against the GenBank database using BLASTA/BLASTX and FASTA search protocols. The search revealed at least some identity with an EST reported by the I.M.A.G.E. Consortium identified as "yo68a05.r1 Homo sapiens cDNA clone 183056 5'" (GenBank accession number H42936). The search also found a hit at GenBank accession number H42872. The human cDNA clone corresponding to the EST database entry was ordered from Genome Systems, Inc., St. Louis, Mo, a distributor of the I.M.A.G.E. Consortium library. The clone received from the distributor was examined and determined to be a full length clone, including a 5' end and 3' UTR (including a polyA tail). This full-length clone is also referred to herein as "AM340".

Applicants' methods identified clone AM340 as encoding a secreted protein.

The nucleotide sequence of AM340 as presently determined is reported in SEQ ID NO:9. What applicants believe is the proper reading frame and the predicted amino acid sequence of the full length AM340 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:10. .

Protein "AM282"

One protein of the present invention has been identified as protein "AM282". A partial cDNA clone encoding AM282 was first isolated from a human fetal kidney cDNA library using methods which are selective for cDNAs encoding secreted proteins. The nucleotide sequence of such partial cDNA was determined and searched against the GenBank database using BLASTA/BLASTX and FASTA search protocols. The search revealed at least some identity with an EST reported by the I.M.A.G.E. Consortium identified as "yf95b10.r1 Human EST 30142 5'" (GenBank accession number R18560). The search also found a thiat GenBank accession number T96696. The human cDNA clone corresponding to the EST database entry was ordered from Genome Systems, Inc., St. Louis, Mo, a distributor of the I.M.A.G.E. Consortium library. The clone received from the distributor was examined and determined to be a full length clone, including a 5' end and 3' UTR (including a polyA tail). This full-length clone is also referred to herein as "AM282".

Applicants' methods identified clone AM282 as encoding a secreted protein.

The nucleotide sequence of the 5' portion of AM282 as presently determined is reported in SEQ ID NO:11. What applicants believe is the proper reading frame and the predicted N-terminal amino acid sequence of the full length AM282 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:12. Amino acids 1 to 24 are the predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 25. Additional nucleotide sequence from the 3' portion of AM282, including the polyA tail, is reported in SEQ ID NO:13.

Protein "AK647"

One protein of the present invention has been identified as protein "AK647". A partial cDNA clone encoding AK647 was first isolated from a human fetal kidney cDNA library using methods which are selective for cDNAs encoding secreted proteins. The nucleotide sequence of such partial cDNA was determined and searched against the GenBank database using BLASTA/BLASTX and FASTA search protocols. The search revealed at least some identity with an EST reported by the I.M.A.G.E. Consortium identified as "ym40a05.r1 Human EST 50483 5'" (GenBank accession number H17726).

The human cDNA clone corresponding to the EST database entry was ordered from Genome Systems, Inc., St. Louis, Mo, a distributor of the I.M.A.G.E. Consortium library. The clone received from the distributor was examined and determined to be a full length clone, including a 5' end and 3' UTR (including a polyA tail). This full-length clone is also referred to herein as "AK647".

Applicants' methods identified clone AK647 as encoding a secreted protein.

The nucleotide sequence of the 5' portion of AK647 as presently determined is reported in SEQ ID NO:14. What applicants believe is the proper reading frame and the predicted N-terminal amino acid sequence of the full length AK647 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:15. Amino acids 1 to 25 are the predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 26. Additional nucleotide sequence from the 3' portion of AK647, including the polyA tail, is reported in SEQ ID NO:16.

Protein "AK583"

One protein of the present invention has been identified as protein "AK583". A partial cDNA clone encoding AK583 was first isolated from a human fetal kidney cDNA library using methods which are selective for cDNAs encoding secreted proteins. The nucleotide sequence of such partial cDNA was determined and searched against the GenBank database using BLASTA/BLASTX and FASTA search protocols. The search revealed at least some identity with an EST reported by the I.M.A.G.E. Consortium identified as "yi90c06.r1 Human EST 14656 5'" (GenBank accession number R77830). The search also found a hit at GenBank accession number H45398. The human cDNA clone corresponding to the EST database entry was ordered from Genome Systems, Inc., St. Louis, Mo, a distributor of the I.M.A.G.E. Consortium library. The clone received from the distributor was examined and determined to be a full length clone, including a 5' end and 3' UTR (including a polyA tail). This full-length clone is also referred to herein as "AK583".

Applicants' methods identified clone AK583 as encoding a secreted protein.

The nucleotide sequence of the 5' portion of AK583 as presently determined is reported in SEQ ID NO:17. What applicants believe is the proper reading frame and the predicted N-terminal amino acid sequence of the full length AK583 protein corresponding

to the foreg ing nucleotide sequence is reported in SEQ ID NO:18. Amino acids 1 to 24 are the predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 25. Additional nucleotide sequence from the 3' portion of AK583, including the polyA tail, is reported in SEQ ID NO:19.

Protein "AK533"

One protein of the present invention has been identified as protein "AK533". A partial cDNA clone encoding AK533 was first isolated from a human fetal kidney cDNA library using methods which are selective for cDNAs encoding secreted proteins. The nucleotide sequence of such partial cDNA was determined and searched against the GenBank database using BLASTA/BLASTX and FASTA search protocols. The search revealed at least some identity with an EST reported by the I.M.A.G.E. Consortium identified as "yb82h07.r1 Homo sapiens cDNA clone 77725 5'" (GenBank accession number T55939). The human cDNA clone corresponding to the EST database entry was ordered from Genome Systems, Inc., St. Louis, Mo, a distributor of the I.M.A.G.E. Consortium library. The clone received from the distributor was examined and determined to be a full length clone, including a 5' end and 3' UTR (including a polyA tail). This full-length clone is also referred to herein as "AK533".

Applicants' methods identified clone AK533 as encoding a secreted protein.

The nucleotide sequence of the 5' portion of AK533 as presently determined is reported in SEQ ID NO:20. What applicants believe is the proper reading frame and the predicted N-terminal amino acid sequence of the full length AK533 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:21. Additional nucleotide sequence from the 3' portion of AK533, including the polyA tail, is reported in SEQ ID NO:22.

Protein "AK296"

One protein of the present invention has been identified as protein "AK296". A partial cDNA clone encoding AK296 was first isolated from a human fetal kidney cDNA library using methods which are selective for cDNAs encoding secreted proteins. The

nucleotide sequence f such partial cDNA was determined and searched against the GenBank database using BLASTA/BLASTX and FASTA search protocols. The search revealed at least some identity with an EST reported by the I.M.A.G.E. Consortium identified as "yc86g12.r1 Homo sapeins cDNA clone 22958 5'" (GenBank accession number T75226). The human cDNA clone corresponding to the EST database entry was ordered from Genome Systems, Inc., St. Louis, Mo, a distributor of the I.M.A.G.E. Consortium library. The clone received from the distributor was examined and determined to be a full length clone, including a 5' end and 3' UTR (including a polyA tail). This full-length clone is also referred to herein as "AK296".

Applicants' methods identified clone AK296 as encoding a secreted protein.

The nucleotide sequence of the 5' portion of AK296 as presently determined is reported in SEQ ID NO:23. What applicants believe is the proper reading frame and the predicted N-terminal amino acid sequence of the full length AK296 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:24. Amino acids 1 to 36 are the predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 37. Additional nucleotide sequence from the 3' portion of AK296, including the polyA tail, is reported in SEQ ID NO:25.

Protein "H617"

One protein of the present invention has been identified as protein "H617". A partial cDNA clone encoding H617 was first isolated from a human PBMC cDNA library using methods which are selective for cDNAs encoding secreted proteins. The nucleotide sequence of such partial cDNA was determined and searched against the GenBank database using BLASTA/BLASTX and FASTA search protocols. The search revealed at least some identity with an EST reported by the I.M.A.G.E. Consortium identified as "ys11c12.r1 Homo sapeins cDNA clone 214486 5'" (GenBank accession number H71514). The search also found a hit at GenBank accession number R10010. The human cDNA clone corresponding to the EST database entry was ordered from Genome Systems, Inc., St. Louis, Mo, a distributor of the I.M.A.G.E. Consortium library. The clone received from the distributor was examined and determined to be a full length clone, including a 5' end and 3' UTR (including a polyA tail). This full-length clone is also referred to herein as "H617".

Applicants' methods identified clone H617 as encoding a secreted protein.

The nucleotide sequence of the 5' portion of H617 as presently determined is reported in SEQ ID NO:26. What applicants believe is the proper reading frame and the predicted N-terminal amino acid sequence of the full length H617 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:27. Additional nucleotide sequence from the 3' portion of H617, including the polyA tail, is reported in SEQ ID NO:28.

Protein "BB9"

One protein of the present invention has been identified as protein "BB9". A partial cDNA clone encoding BB9 was first isolated from a human PBMC (TH1 or Th2) cDNA library using methods which are selective for cDNAs encoding secreted proteins. The nucleotide sequence of such partial cDNA was determined and searched against the GenBank database using BLASTA/BLASTX and FASTA search protocols. The search revealed at least some identity with an EST reported by the I.M.A.G.E. Consortium identified as "yd68g04.r1 Human cDNA clone 113430 5'" (GenBank accession number T78562). The search also found a thi at GenBank accession number R54388. The human cDNA clone corresponding to the EST database entry was ordered from Genome Systems, Inc., St. Louis, Mo, a distributor of the I.M.A.G.E. Consortium library. The clone received from the distributor was examined and determined to be a full length clone, including a 5' end and 3' UTR (including a polyA tail). This full-length clone is also referred to herein as "BB9".

Applicants' methods identified clone BB9 as encoding a secreted protein.

The nucleotide sequence of the 5' portion of BB9 as presently determined is reported in SEQ ID NO:29. What applicants believe is the proper reading frame and the predicted N-terminal amino acid sequence of the full length BB9 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:30. Additional nucleotide sequence from the 3' portion of BB9, including the polyA tail, is reported in SEQ ID NO:31.

Protein "AW191"

One protein of the present invention has been identified as protein "AW191". A partial cDNA clone encoding AW191 was first isolated from a human ovary (PA-1 teratocarcinoma) cDNA library using methods which are selective for cDNAs encoding secreted proteins. The nucleotide sequence of such partial cDNA was determined and searched against the GenBank database using BLASTA/BLASTX and FASTA search protocols. The search revealed at least some identity with an EST reported by the I.M.A.G.E. Consortium identified as "ym03d10.r1 Homo sapiens cDNA clone 46942 5'" (GenBank accession number H10314. The search also found a hit at GenBank accession number H05460. The human cDNA clone corresponding to the EST database entry was ordered from Genome Systems, Inc., St. Louis, Mo, a distributor of the I.M.A.G.E. Consortium library. The clone received from the distributor was examined and determined to be a full length clone, including a 5' end and 3' UTR (including a polyA tail). This full-length clone is also referred to herein as "AW191".

Applicants' methods identified clone AW191 as encoding a secreted protein.

The nucleotide sequence of the 5' portion of AW191 as presently determined is reported in SEQ ID NO:32. What applicants believe is the proper reading frame and the predicted N-terminal amino acid sequence of the full length AW191 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:33. Amino acids 1 to 18 are the predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 19. Additional nucleotide sequence from the 3' portion of AW191, including the polyA tail, is reported in SEQ ID NO:34.

Protein "AT211"

One protein of the present invention has been identified as protein "AT211". A partial cDNA clone encoding AT211 was first isolated from a human lymphocyte and dendritic cell cDNA library using methods which are selective for cDNAs encoding secreted proteins. The nucleotide sequence of such partial cDNA was determined and searched against the GenBank database using BLASTA/BLASTX and FASTA search protocols. The search revealed at least some identity with an EST reported by the I.M.A.G.E. Consortium identified as "yq36f01.r1 Homo sapiens cDNA clone 197881 5'" (GenBank accession number R96278). The search also found a hit at GenBank accession

number R56077. The human cDNA clone corresponding to the EST database entry was ordered from Genome Systems, Inc., St. Louis, Mo, a distributor of the I.M.A.G.E. Consortium library. The clone received from the distributor was examined and determined to be a full length clone, including a 5' end and 3' UTR (including a polyA tail). This full-length clone is also referred to herein as "AT211".

Applicants' methods identified clone AT211 as encoding a secreted protein.

The nucleotide sequence of the 5' portion of AT211 as presently determined is reported in SEQ ID NO:35. What applicants believe is the proper reading frame and the predicted N-terminal amino acid sequence of the full length AT211 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:36. Amino acids 1 to 53 are the predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 54. Additional nucleotide sequence from the 3' portion of AT211, including the polyA tail, is reported in SEQ ID NO:37.

Protein "AT205"

One protein of the present invention has been identified as protein "AT205". A partial cDNA clone encoding AT205 was first isolated from a human lymphocyte and dendritic cell cDNA library using methods which are selective for cDNAs encoding secreted proteins. The nucleotide sequence of such partial cDNA was determined and searched against the GenBank database using BLASTA/BLASTX and FASTA search protocols. The search revealed at least some identity with an EST reported by the I.M.A.G.E. Consortium identified as "yu83c11.r1 Homo sapiens cDNA clone 240404 5'" (GenBank accession number H78080). The search also found a hit at GenBank accession number H78081. The human cDNA clone corresponding to the EST database entry was ordered from Genome Systems, Inc., St. Louis, Mo, a distributor of the I.M.A.G.E. Consortium library. The clone received from the distributor was examined and determined to be a full length clone, including a 5' end and 3' UTR (including a polyA tail). This full-length clone is also referred to herein as "AT205".

Applicants' methods identified clone AT205 as encoding a secreted protein.

The nucleotide sequence of AT205 as presently determined is reported in SEQ ID NO:38. What applicants believe is the proper reading frame and the predicted amino acid sequence of the full length AT205 protein corresponding to the foregoing nucleotide

sequence is reported in SEQ ID NO:39. Amino acids 1 to 55 are the predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 56.

Protein "AS34"

One protein of the present invention has been identified as protein "AS34". A partial cDNA clone encoding AS34 was first isolated from a human fetal brain cDNA library using methods which are selective for cDNAs encoding secreted proteins. The nucleotide sequence of such partial cDNA was determined and searched against the GenBank database using BLASTA/BLASTX and FASTA search protocols. The search revealed at least some identity with an EST reported by the I.M.A.G.E. Consortium identified as "yg71a01.r1 Homo sapiens cDNA clone 38531 5'" (GenBank accession number R51118). The search also found a hit at GenBank accession number R15801. The human cDNA clone corresponding to the EST database entry was ordered from Genome Systems, Inc., St. Louis, Mo, a distributor of the I.M.A.G.E. Consortium library. The clone received from the distributor was examined and determined to be a full length clone, including a 5' end and 3' UTR (including a polyA tail). This full-length clone is also referred to herein as "AS34".

Applicants' methods identified clone AS34 as encoding a secreted protein.

The nucleotide sequence of the 5' portion of AS34 as presently determined is reported in SEQ ID NO:40. What applicants believe is the proper reading frame and the predicted N-terminal amino acid sequence of the full length AS34 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:41. Amino acids 1 to 24 are the predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 25. Additional nucleotide sequence from the 3' portion of AS34, including the polyA tail, is reported in SEQ ID NO:42.

Protein "AS32"

One protein of the present invention has been identified as protein "AS32". A partial cDNA clone encoding AS32 was first isolated from a human fetal brain cDNA library using methods which are selective for cDNAs encoding secreted proteins. The

nucleotide sequence of such partial cDNA was determined and searched against the GenBank database using BLASTA/BLASTX and FASTA search protocols. The search revealed at least some identity with an EST reported by the I.M.A.G.E. Consortium identified as "yu75b08.r1 Homo sapiens cDNA clone 239607 5'" (GenBank accession number H80466). The search also found a hit at GenBank accession number H77627. The human cDNA clone corresponding to the EST database entry was ordered from Genome Systems, Inc., St. Louis, Mo, a distributor of the I.M.A.G.E. Consortium library. The clone received from the distributor was examined and determined to be a full length clone, including a 5' end and 3' UTR (including a polyA tail). This full-length clone is also referred to herein as "AS32".

Applicants' methods identified clone AS32 as encoding a secreted protein.

The nucleotide sequence of the 5' portion of AS32 as presently determined is reported in SEQ ID NO:43. What applicants believe is the proper reading frame and the predicted N-terminal amino acid sequence of the full length AS32 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:44. Additional nucleotide sequence from the 3' portion of AS32, including the polyA tail, is reported in SEQ ID NO:45.

Protein "AR260"

One protein of the present invention has been identified as protein "AR260". A partial cDNA clone encoding AR260 was first isolated from a human adult retina cDNA library using methods which are selective for cDNAs encoding secreted proteins. The nucleotide sequence of such partial cDNA was determined and searched against the GenBank database using BLASTA/BLASTX and FASTA search protocols. The search revealed at least some identity with an EST reported by the I.M.A.G.E. Consortium identified as "yg99g12.r1 Homo sapiens cDNA clone 41757 5'" (GenBank accession number R52804). The human cDNA clone corresponding to the EST database entry was ordered from Genome Systems, Inc., St. Louis, Mo. a distributor of the I.M.A.G.E. Consortium library. The clone received from the distributor was examined and determined to be a full length clone, including a 5' end and 3' UTR (including a polyA tail). This full-length clone is also referred to herein as "AR260".

Applicants' methods identified clone AR260 as encoding a secreted protein.

The nucleotide sequence of the 5' portion of AR260 as presently determined is reported in SEQ ID NO:46. What applicants believe is the proper reading frame and the predicted N-terminal amino acid sequence of the full length AR260 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:47. Amino acids 1 to 23 are the predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 24. Additional nucleotide sequence from the 3' portion of AR260, including the polyA tail, is reported in SEQ ID NO:48.

Protein "K640"

One protein of the present invention has been identified as protein "K640". A partial cDNA clone encoding K640 was first isolated from a murine bone marrow (stromal cell line FCM-4) cDNA library using methods which are selective for cDNAs encoding secreted proteins. The nucleotide sequence of such partial cDNA was determined and searched against the GenBank database using BLASTA/BLASTX and FASTA search protocols. The search revealed at least some identity with an EST reported by the I.M.A.G.E. Consortium identified as "yf47a09.r1 Homo sapiens cDNA clone 129976 5'" (GenBank accession number R11595). The search also found a hit at GenBank accession number H09031. The human cDNA clone corresponding to the EST database entry was ordered from Genome Systems, Inc., St. Louis, Mo, a distributor of the I.M.A.G.E. Consortium library. The clone received from the distributor was examined and determined to be a full length clone, including a 5' end and 3' UTR (including a polyA tail). This full-length clone is also referred to herein as "K640".

Applicants' methods identified clone K640 as encoding a secreted protein.

The nucleotide sequence of the 5' portion of K640 as presently determined is reported in SEQ ID NO:49. What applicants believe is the proper reading frame and the predicted N-terminal amino acid sequence of the full length K640 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:50. Additional nucleotide sequence from the 3' portion of K640, including the polyA tail, is reported in SEQ ID NO:51.

Protein "K39"

One protein of the present invention has been identified as protein "K39". A partial cDNA clone encoding K39 was first isolated from a murine bone marrow (stromal cell line FCM-4) cDNA library using methods which are selective for cDNAs encoding secreted proteins. The nucleotide sequence of such partial cDNA was determined and searched against the GenBank database using BLASTA/BLASTX and FASTA search protocols. The search revealed at least some identity with an EST reported by the I.M.A.G.E. Consortium identified as "ym65b04.r1 Homo sapiens cDNA clone 163759 5'" (GenBank accession number H14129). The search also found a hit at GenBank accession number H68304. The human cDNA clone corresponding to the EST database entry was ordered from Genome Systems, Inc., St. Louis, Mo, a distributor of the I.M.A.G.E. Consortium library. The clone received from the distributor was examined and determined to be a full length clone, including a 5' end and 3' UTR (including a polyA tail). This full-length clone is also referred to herein as "K39".

Applicants' methods identified clone K39 as encoding a secreted protein.

The nucleotide sequence of the 5' portion of K39 as presently determined is reported in SEQ ID NO:52. What applicants believe is the proper reading frame and the predicted N-terminal amino acid sequence of the full length K39 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:53. Additional nucleotide sequence from the 3' portion of K39, including the polyA tail, is reported in SEQ ID NO:54.

Protein "AT319"

One protein of the present invention has been identified as protein "AT319". A partial cDNA clone encoding AT319 was first isolated from a human lymphocyte and dendritic cell cDNA library using methods which are selective for cDNAs encoding secreted proteins. The nucleotide sequence of such partial cDNA was determined and searched against the GenBank database using BLASTA/BLASTX and FASTA search protocols. The search revealed at least some identity with an EST reported by the I.M.A.G.E. Consortium identified as "yr21b11.r1 Homo sapiens cDNA clone 205917 5'" (GenBank accession number H57730). The search also found a hit at GenBank accession number H57731. The human cDNA clone corresponding to the EST database entry was

ordered from Genome Systems, Inc., St. Louis, Mo, a distributor of the I.M.A.G.E. Consortium library. The clone received from the distributor was examined and determined to be a full length clone, including a 5' end and 3' UTR (including a polyA tail). This full-length clone is also referred to herein as "AT319".

Applicants' methods identified clone AT319 as encoding a secreted protein.

The nucleotide sequence of the 5' portion of AT319 as presently determined is reported in SEQ ID NO:55. What applicants believe is the proper reading frame and the predicted N-terminal amino acid sequence of the full length AT319 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:56. Additional nucleotide sequence from the 3' portion of AT319, including the polyA tail, is reported in SEQ ID NO:57.

Deposit of Clones

Clones AP162, AM931, AM610, AM340, AM282, AK647, AK583, AK533, AK296, H617, BB9, AW191, AT211, AT205, AS34, AS32, AR260, K640, K39 and AT319 were deposited on April 17, 1996 with the American Type Culture Collection under accession number ATCC 98026, from which each clone comprising a particular polynucleotide is obtainable. Each clone has been transfected into separate bacterial cells (*E. coli*) in this composite deposit. Bacterial cells containing a particular clone can be obtained from the composite deposit as follows:

An oligonucleotide probe or probes should be designed to the sequence that is known for that particular clone. This sequence can be derived from the sequences provided herein, or from a combination of those sequences.

The design of the oligonucleotide probe should preferably follow these parameters:

(a) It should be designed to an area of the sequence which has the fewest ambiguous bases ("N's"), if any;

(b) It should be designed to have a T_m of approx. 80 ° C (assuming 2° for each A or T and 4 degrees for each G or C).

The oligonucleotide should preferably be labeled with g-^{32}P ATP (specific activity 6000 Ci/mmole) and T4 polynucleotide kinase using commonly employed techniques for labeling oligonucleotides. Other labeling techniques can also be used. Unincorporated label should preferably be removed by gel filtration chromatography or other established methods. The amount of radioactivity incorporated into the probe should be quantitated by measurement in a scintillation counter. Preferably, specific activity of the resulting probe should be approximately 4e+6 dpm/pmole.

The bacterial culture containing the pool of full-length clones should preferably be thawed and 100 µl of the stock used to inoculate a sterile culture flask containing 25 ml of sterile L-broth containing ampicillin at 100 µg/ml. The culture should preferably be grown to saturation at 37°C, and the saturated culture should preferably be diluted in fresh L-broth. Aliquots of these dilutions should preferably be plated to determine the dilution and volume which will yield approximately 5000 distinct and well-separated colonies on solid bacteriological media containing L-broth containing ampicillin at 100 µg/ml and agar at 1.5% in a 150 mm petri dish when grown overnight at 37°C. Other known methods of obtaining distinct, well-separated colonies can also be employed.

Standard colony hybridization procedures should then be used to transfer the colonies to nitrocellulose filters and lyse, denature and bake them.

The filter is then preferably incubated at 65°C for 1 hour with gentle agitation in 6X SSC (20X stock is 175.3 g NaCl/liter, 88.2 g Na citrate/liter, adjusted to pH 7.0 with NaOH) containing 0.5% SDS, 100 μg/ml of yeast RNA, and 10 mM EDTA (approximately 10 mL per 150 mm filter). Preferably, the probe is then added to the hybridization mix at a concentration greater than or equal to 1e+6 dpm/mL. The filter is then preferably incubated at 65°C with gentle agitation overnight. The filter is then preferably washed in 500 mL of 2X SSC/0.5% SDS at room temperature without agitation, preferably followed by 500 mL of 2X SSC/0.1% SDS at room temperature with gentle shaking for 15 minutes. A third wash with 0.1X SSC/0.5% SDS at 65°C for 30 minutes to 1 hour is optional. The filter is then preferably dried and subjected to autoradiography for sufficient time to visualize the positives on the X-ray film. Other known hybridization methods can also be employed.

The positive colonies are picked, grown in culture, and plasmid DNA isolated using standard procedures. The clones can then be verified by restriction analysis, hybridization analysis, or DNA sequencing.

Fragments of the proteins of the present invention which are capable of exhibiting biological activity are also encompassed by the present invention. Fragments of the protein may be in linear form or they may be cyclized using known methods, for example, as described in H.U. Saragovi, *et al.*, Bio/Technology 10, 773-778 (1992) and in R.S. McDowell, *et al.*, J. Amer. Chem. Soc. 114, 9245-9253 (1992), both of which are incorporated herein by reference. Such fragments may be fused to carrier molecules such as immunoglobulins for many purposes, including increasing the valency of protein binding sites. For example, fragments of the protein may be fused through "linker" sequences to the Fc portion of an immunoglobulin. For a bivalent form of the protein, such a fusion could be to the Fc portion of an IgG molecule. Other immunoglobulin isotypes may also be used to generate such fusions. For example, a protein - IgM fusion would generate a decavalent form of the protein of the invention.

The present invention also provides both full-length and mature forms of the disclosed proteins. The full-length form of the such proteins is identified in the sequence listing by translation of the nucleotide sequence of each disclosed clone. The mature form of such protein may be obtained by expression of the disclosed full-length polynucleotide (preferably those deposited with ATCC) in a suitable mammalian cell or other host cell.

The sequence f the mature form f the protein may also be determinable from the amino acid sequence of the full-length form.

Where the protein of the present invention is membrane-bound (e.g., is a receptor), the present invention also provides for soluble forms of such protein. In such forms part or all of the intracellular and transmembrane domains of the protein are deleted such that the protein is fully secreted from the cell in which it is expressed. The intracellular and transmembrane domains of proteins of the invention can be identified in accordance with known techniques for determination of such domains from sequence information.

Species homologs of the disclosed proteins are also provided by the present invention. Species homologs may be isolated and identified by making suitable probes or primers from the sequences provided herein and screening a suitable nucleic acid source from the desired species.

The invention also encompasses allelic variants of the disclosed proteins: that is, naturally-occurring alternative forms of the isolated proteins which are identical, homologous or related to that encoded by the polynucleotides disclosed herein.

The isolated polynucleotide endcoing the protein of the invention may be operably linked to an expression control sequence such as the pMT2 or pED expression vectors disclosed in Kaufman *et al.*, Nucleic Acids Res. 19, 4485-4490 (1991), in order to produce the protein recombinantly. Many suitable expression control sequences are known in the art. General methods of expressing recombinant proteins are also known and are exemplified in R. Kaufman, Methods in Enzymology 185, 537-566 (1990). As defined herein "operably linked" means that the isolated polynucleotide of the invention and an expression control sequence are situated within a vector or cell in such a way that the protein is expressed by a host cell which has been transformed (transfected) with the ligated polynucleotide/expression control sequence.

A number of types of cells may act as suitable host cells for expression of the protein. Mammalian host cells include, for example, monkey COS cells, Chinese Hamster Ovary (CHO) cells, human kidney 293 cells, human epidermal A431 cells, human Colo205 cells, 3T3 cells, CV-1 cells, other transformed primate cell lines, normal diploid cells, cell strains derived from in vitro culture of primary tissue, primary explants, HeLa cells, mouse L cells, BHK, HL-60, U937, HaK or Jurkat cells.

Alternatively, it may be possible to produce the protein in lower eukaryotes such as yeast or in prokaryotes such as bacteria. Potentially suitable yeast strains include *Saccharomyces cerevisiae, Schizosaccharomyces pombe, Kluyveromyces* strains, *Candida,*

or any yeast strain capable of expressing heterologous proteins. Potentially suitable bacterial strains include *Escherichia coli*, *Bacillus subtilis*, *Salmonella typhimurium*, or any bacterial strain capable of expressing heterologous proteins. If the protein is made in yeast or bacteria, it may be necessary to modify the protein produced therein, for example by phosphorylation or glycosylation of the appropriate sites, in order to obtain the functional protein. Such covalent attachments may be accomplished using known chemical or enzymatic methods.

The protein may also be produced by operably linking the isolated polynucleotide of the invention to suitable control sequences in one or more insect expression vectors, and employing an insect expression system. Materials and methods for baculovirus/insect cell expression systems are commercially available in kit form from, *e.g.*, Invitrogen, San Diego, California, U.S.A. (the MaxBac® kit), and such methods are well known in the art, as described in Summers and Smith, Texas Agricultural Experiment Station Bulletin No. 1555 (1987), incorporated herein by reference. As used herein, an insect cell capable of expressing a polynucleotide of the present invention is "transformed."

The protein of the invention may be prepared by culturing transformed host cells under culture conditions suitable to express the recombinant protein. The resulting expressed protein may then be purified from such culture (i.e., from culture medium or cell extracts) using known purification processes, such as gel filtration and ion exchange chromatography. The purification of the protein may also include an affinity column containing agents which will bind to the protein; one or more column steps over such affinity resins as concanavalin A-agarose, heparin-toyopearl® or Cibacrom blue 3GA Sepharose®; one or more steps involving hydrophobic interaction chromatography using such resins as phenyl ether, butyl ether, or propyl ether; or immunoaffinity chromatography.

Alternatively, the protein of the invention may also be expressed in a form which will facilitate purification. For example, it may be expressed as a fusion protein, such as those of maltose binding protein (MBP), glutathione-S-transferase (GST) or thioredoxin (TRX). Kits for expression and purification of such fusion proteins are commercially available from New England BioLab (Beverly, MA), Pharmacia (Piscataway, NJ) and InVitrogen, respectively. The protein can also be tagged with an epitope and subsequently purified by using a specific antibody directed to such epitope. One such epitope ("Flag") is commercially available from Kodak (New Haven, CT).

Finally, one or more reverse-phase high performance liquid chromatography (RP-HPLC) steps employing hydrophobic RP-HPLC media, e.g., silica gel having pendant methyl or other aliphatic groups, can be employed to further purify the protein. Some or all of the foregoing purification steps, in various combinations, can also be employed to provide a substantially homogeneous isolated recombinant protein. The protein thus purified is substantially free of other mammalian proteins and is defined in accordance with the present invention as an "isolated protein."

The protein of the invention may also be expressed as a product of transgenic animals, e.g., as a component of the milk of transgenic cows, goats, pigs, or sheep which are characterized by somatic or germ cells containing a nucleotide sequence encoding the protein.

The protein may also be produced by known conventional chemical synthesis. Methods for constructing the proteins of the present invention by synthetic means are known to those skilled in the art. The synthetically-constructedprotein sequences, by virtue of sharing primary, secondary or tertiary structural and/or conformational characteristics with proteins may possess biological properties in common therewith, including protein activity. Thus, they may be employed as biologically active or immunological substitutes for natural, purified proteins in screening of therapeutic compounds and in immunological processes for the development of antibodies.

The proteins provided herein also include proteins characterized by amino acid sequences similar to those of purified proteins but into which modification are naturally provided or deliberately engineered. For example, modifications in the peptide or DNA sequences can be made by those skilled in the art using known techniques. Modifications of interest in the protein sequences may include the alteration, substitution, replacement, insertion or deletion of a selected amino acid residue in the coding sequence. For example, one or more of the cysteine residues may be deleted or replaced with another amino acid to alter the conformation of the molecule. Techniques for such alteration, substitution, replacement, insertion or deletion are well known to those skilled in the art (see, e.g., U.S. Patent No. 4,518,584). Preferably, such alteration, substitution, replacement, insertion or deletion retains the desired activity of the protein.

Other fragments and derivatives of the sequences of proteins which would be expected to retain protein activity in whole or in part and may thus be useful for screening or other immunological methodologies may also be easily made by those skilled in the art

given the disclosures herein. Such modifications are believed to be encompassed by the present inventi n.

USES AND BIOLOGICAL ACTIVITY

The proteins of the present invention are expected to exhibit one or more of the uses or biological activities (including those associated with assays cited herein) identified below. Uses or activities described for proteins of the present invention may be provided by administration or use of such proteins or by administration or use of polynucleotides encoding such proteins (such as, for example, in gene therapies or vectors suitable for introduction of DNA).

Research Uses and Utilities

The proteins provided by the present invention can similarly be used in assay to determine biological activity, including in a panel of multiple proteins for high-throughput screening; to raise antibodies or to elicit another immune response; as a reagent (including the labeled reagent) in assays designed to quantitatively determine levels of the protein (or its receptor) in biological fluids; as markers for tissues in which the corresponding protein is preferentially expressed (either constitutively or at a particular stage of tissue differentiation or development or in a disease state); and, of course, to isolate correlative receptors or ligands. Where the protein binds or potentially binds to another protein (such as, for example, in a receptor-ligand interaction), the protein can be used to identify the other protein with which binding occurs or to identify inhibitors of the binding interaction. Proteins involved in these binding interactions can also be used to screen for peptide or small molecule inhibitors or agonists of the binding interaction.

Any or all of these research utilities are capable of being developed into reagent grade or kit format for commercialization as research products.

Methods for performing the uses listed above are well known to those skilled in the art. References disclosing such methods include without limitation "Molecular Cloning: A Laboratory Manual", 2d ed., Cold Spring Harbor Laboratory Press, Sambrook, J., E.F. Fritsch and T. Maniatis eds., 1989, and "Methods in Enzymology: Guide to Molecular Cloning Techniques", Academic Press, Berger, S.L. and A.R. Kimmel eds., 1987.

Nutritional Uses

Proteins of the present invention can also be used as nutritional sources or supplements. Such uses include without limitation use as a protein or amino acid supplement, use as a carbon source, use as a nitrogen source and use as a source of carbohydrate. In such cases the protein of the invention can be added to the feed of a particular organism or can be administered as a separate solid or liquid preparation, such as in the form of powder, pills, solutions, suspensions or capsules. In the case of microorganisms, the protein of the invention can be added to the medium in or on which the microorganism is cultured.

Cytokine and Cell Proliferation/Differentiation Activity

A protein of the present invention may exhibit cytokine, cell proliferation (either inducing or inhibiting) or cell differentiation (either inducing or inhibiting) activity or may induce production of other cytokines in certain cell populations. Many protein factors discovered to date, including all known cytokines, have exhibited activity in one or more factor dependent cell proliferation assays, and hence the assays serve as a convenient confirmation of cytokine activity. The activity of a protein of the present invention is evidenced by any one of a number of routine factor dependent cell proliferation assays for cell lines including, without limitation, 32D, DA2, DA1G, T10, B9, B9/11, BaF3, MC9/G, M+ (preB M+), 2E8, RB5, DA1, 123, T1165, HT2, CTLL2, TF-1, Mo7e and CMK.

The activity of a protein of the invention may, among other means, be measured by the following methods:

Assays for T-cell or thymocyte proliferation include without limitation those described in: Current Protocols in Immunology, Ed by J. E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, In Vitro assays for Mouse Lymphocyte Function 3.1-3.19; Chapter 7, Immunologic studies in Humans); Takai et al., J. Immunol. 137:3494-3500, 1986; Bertagnolli et al., J. Immunol. 145:1706-1712, 1990; Bertagnolli et al., Cellular Immunology 133:327-341, 1991; Bertagnolli, et al., J. Immunol. 149:3778-3783, 1992; Bowman et al., J. Immunol. 152: 1756-1761, 1994.

Assays for cytokine production and/or proliferation of spleen cells, lymph node cells or thymocytes include, without limitation, those described in: Polyclonal T cell stimulation, Kruisbeek, A.M. and Shevach, E.M. In *Current Protocols in Immunology*. J.E.e.a. Coligan eds. Vol 1 pp. 3.12.1-3.12.14, John Wiley and Sons, Toronto. 1994; and Measurement of mouse and human Interferon γ, Schreiber, R.D. In *Current Protocols in*

Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 6.8.1-6.8.8, John Wiley and Sons, Toronto. 1994.

Assays for proliferation and differentiation of hematopoietic and lymphopoietic cells include, without limitation, those described in: Measurement of Human and Murine Interleukin 2 and Interleukin 4, Bottomly, K., Davis, L.S. and Lipsky, P.E. In *Current Protocols in Immunology*. J.E.e.a. Coligan eds. Vol 1 pp. 6.3.1-6.3.12, John Wiley and Sons, Toronto. 1991; deVries et al., J. Exp. Med. 173:1205-1211, 1991; Moreau et al., Nature 336:690-692, 1988; Greenberger et al., Proc. Natl. Acad. Sci. U.S.A. 80:2931-2938, 1983; Measurement of mouse and human interleukin 6 - Nordan, R. In *Current Protocols in Immunology*. J.E.e.a. Coligan eds. Vol 1 pp. 6.6.1-6.6.5, John Wiley and Sons, Toronto. 1991; Smith et al., Proc. Natl. Acad. Sci. U.S.A. 83:1857-1861, 1986; Measurement of human Interleukin 11 - Bennett, F., Giannotti, J., Clark, S.C. and Turner, K. J. In *Current Protocols in Immunology*. J.E.e.a. Coligan eds. Vol 1 pp. 6.15.1 John Wiley and Sons, Toronto. 1991; Measurement of mouse and human Interleukin 9 - Ciarletta, A., Giannotti, J., Clark, S.C. and Turner, K.J. In *Current Protocols in Immunology*. J.E.e.a. Coligan eds. Vol 1 pp. 6.13.1, John Wiley and Sons, Toronto. 1991.

Assays for T-cell clone responses to antigens (which will identify, among others, proteins that affect APC-T cell interactions as well as direct T-cell effects by measuring proliferation and cytokine production) include, without limitation, those described in: Current Protocols in Immunology, Ed by J. E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, In Vitro assays for Mouse Lymphocyte Function; Chapter 6, Cytokines and their cellular receptors; Chapter 7, Immunologic studies in Humans); Weinberger et al., Proc. Natl. Acad. Sci. USA 77:6091-6095, 1980; Weinberger et al., Eur. J. Immun. 11:405-411, 1981; Takai et al., J. Immunol. 137:3494-3500, 1986; Takai et al., J. Immunol. 140:508-512, 1988.

Immune Stimulating or Suppressing Activity

A protein of the present invention may also exhibit immune stimulating or immune suppressing activity, including without limitation the activities for which assays are described herein. A protein may be useful in the treatment of various immune deficiencies and disorders (including severe combined immunodeficiency (SCID)), e.g., in regulating (up or down) growth and proliferation of T and/or B lymphocytes, as well as effecting the cytolytic activity of NK cells and other cell populations. These immune deficiencies may

be genetic or be caused by viral (e.g., HIV) as well as bacterial or fungal infections, or may result from autoimmune disorders. More specifically, infectious diseases causes by viral, bacterial, fungal or other infection may be treatable using a protein of the present invention, including infections by HIV, hepatitis viruses, herpesviruses, mycobacteria, Leishmania spp., malaria spp. and various fungal infections such as candidiasis. Of course, in this regard, a protein of the present invention may also be useful where a boost to the immune system generally may be desirable, *i.e.*, in the treatment of cancer.

Autoimmune disorders which may be treated using a protein of the present invention include, for example, connective tissue disease, multiple sclerosis, systemic lupus erythematosus, rheumatoid arthritis, autoimmune pulmonary inflammation, Guillain-Barre syndrome, autoimmune thyroiditis, insulin dependent diabetes mellitis, myasthenia gravis, graft-versus-host disease and autoimmune inflammatory eye disease. Such a protein of the present invention may also to be useful in the treatment of allergic reactions and conditions, such as asthma (particularly allergic asthma) or other respiratory problems. Other conditions, in which immune suppression is desired (including, for example, organ transplantation), may also be treatable using a protein of the present invention.

Using the proteins of the invention it may also be possible to immune responses, in a number of ways. Down regulation may be in the form of inhibiting or blocking an immune response already in progress or may involve preventing the induction of an immune response. The functions of activated T cells may be inhibited by suppressing T cell responses or by inducing specific tolerance in T cells, or both. Immunosuppression of T cell responses is generally an active, non-antigen-specific, process which requires continuous exposure of the T cells to the suppressive agent. Tolerance, which involves inducing non-responsiveness or anergy in T cells, is distinguishable from immunosuppression in that it is generally antigen-specific and persists after exposure to the tolerizing agent has ceased. Operationally, tolerance can be demonstrated by the lack of a T cell response upon reexposure to specific antigen in the absence of the tolerizing agent.

Down regulating or preventing one or more antigen functions (including without limitation B lymphocyte antigen functions (such as , for example, B7)), *e.g.*, preventing high level lymphokine synthesis by activated T cells, will be useful in situations of tissue, skin and organ transplantation and in graft-versus-host disease (GVHD). For example, blockage of T cell function should result in reduced tissue destruction in tissue transplantation. Typically, in tissue transplants, rejection of the transplant is initiated through its recognition as foreign by T cells, followed by an immune reaction that destroys

the transplant. The administration of a molecule which inhibits or blocks interaction of a B7 lymphocyte antigen with its natural ligand(s) on immune cells (such as a soluble, monomeric form of a peptide having B7-2 activity alone or in conjunction with a monomeric form of a peptide having an activity of another B lymphocyte antigen (*e.g.*, B7-1, B7-3) or blocking antibody), prior to transplantation can lead to the binding of the molecule to the natural ligand(s) on the immune cells without transmitting the corresponding costimulatory signal. Blocking B lymphocyte antigen function in this matter prevents cytokine synthesis by immune cells, such as T cells, and thus acts as an immunosuppressant Moreover, the lack of costimulation may also be sufficient to anergize the T cells, thereby inducing tolerance in a subject. Induction of long-term tolerance by B lymphocyte antigen-blocking reagents may avoid the necessity of repeated administration of these blocking reagents. To achieve sufficient immunosuppression or tolerance in a subject, it may also be necessary to block the function of a combination of B lymphocyte antigens.

The efficacy of particular blocking reagents in preventing organ transplant rejection or GVHD can be assessed using animal models that are predictive of efficacy in humans. Examples of appropriate systems which can be used include allogeneic cardiac grafts in rats and xenogeneic pancreatic islet cell grafts in mice, both of which have been used to examine the immunosuppressive effects of CTLA4Ig fusion proteins *in vivo* as described in Lenschow *et al.*, Science *257*:789-792 (1992) and Turka *et al.*, Proc. Natl. Acad. Sci USA, *89*:11102-11105 (1992). In addition, murine models of GVHD (see Paul ed., Fundamental Immunology, Raven Press, New York, 1989, pp. 846-847) can be used to determine the effect of blocking B lymphocyte antigen function *in vivo* on the development of that disease.

Blocking antigen function may also be therapeutically useful for treating autoimmune diseases. Many autoimmune disorders are the result of inappropriate activation of T cells that are reactive against self tissue and which promote the production of cytokines and autoantibodies involved in the pathology of the diseases. Preventing the activation of autoreactive T cells may reduce or eliminate disease symptoms. Administration of reagents which block costimulation of T cells by disrupting receptor:ligand interactions of B lymphocyte antigens can be used to inhibit T cell activation and prevent production of autoantibodies or T cell-derived cytokines which may be involved in the disease process. Additionally, blocking reagents may induce antigen-specific tolerance of autoreactive T cells which could lead to long-term relief from the disease. The efficacy of blocking reagents in preventing or alleviating autoimmune disorders can be determined using a number of

well-characterized animal models of human autoimmune diseases. Examples include murine experimental autoimmune encephalitis, systemic lupus erythmatosis in MRL/*lpr/lpr* mice or NZB hybrid mice, murine autoimmune collagen arthritis, diabetes mellitus in NOD mice and BB rats, and murine experimental myasthenia gravis (see Paul ed., Fundamental Immunology, Raven Press, New York, 1989, pp. 840-856).

Upregulation of an antigen function (preferably a B lymphocyte antigen function), as a means of up regulating immune responses, may also be useful in therapy. Upregulation of immune responses may be in the form of enhancing an existing immune response or eliciting an initial immune response. For example, enhancing an immune response through stimulating B lymphocyte antigen function may be useful in cases of viral infection. In addition, systemic viral diseases such as influenza, the common cold, and encephalitis might be alleviated by the administration of stimulatory forms of B lymphocyte antigens systemically.

Alternatively, anti-viral immune responses may be enhanced in an infected patient by removing T cells from the patient, costimulating the T cells *in vitro* with viral antigen-pulsed APCs either expressing a peptide of the present invention or together with a stimulatory form of a soluble peptide of the present invention and reintroducing the *in vitro* activated T cells into the patient. Another method of enhancing anti-viral immune responses would be to isolate infected cells from a patient, transfect them with a nucleic acid encoding a protein of the present invention as described herein such that the cells express all or a portion of the protein on their surface, and reintroduce the transfected cells into the patient. The infected cells would now be capable of delivering a costimulatory signal to, and thereby activate, T cells *in vivo*.

In another application, up regulation or enhancement of antigen function (preferably B lymphocyte antigen function) may be useful in the induction of tumor immunity. Tumor cells (*e.g.*, sarcoma, melanoma, lymphoma, leukemia, neuroblastoma, carcinoma) transfected with a nucleic acid encoding at least one peptide of the present invention can be administered to a subject to overcome tumor-specific tolerance in the subject. If desired, the tumor cell can be transfected to express a combination of peptides . For example, tumor cells obtained from a patient can be transfected *ex vivo* with an expression vector directing the expression of a peptide having B7-2-like activity alone, or in conjunction with a peptide having B7-1-like activity and/or B7-3-like activity. The transfected tumor cells are returned to the patient to result in expression of the peptides on the surface of the

transfected cell. Alternatively, gene therapy techniques can be used to target a tumor cell for transfection *in vivo*.

The presence of the peptide of the present invention having the activity of a B lymphocyte antigen(s) on the surface of the tumor cell provides the necessary costimulation signal to T cells to induce a T cell mediated immune response against the transfected tumor cells. In addition, tumor cells which lack MHC class I or MHC class II molecules, or which fail to reexpress sufficient amounts of MHC class I or MHC class II molecules, can be transfected with nucleic acid encoding all or a portion of (*e.g.*, a cytoplasmic-domain truncated portion) of an MHC class I α chain protein and β_1 microglobulin protein or an MHC class II α chain protein and an MHC class II β chain protein to thereby express MHC class I or MHC class II proteins on the cell surface. Expression of the appropriate class I or class II MHC in conjunction with a peptide having the activity of a B lymphocyte antigen (*e.g.*,B7-1, B7-2, B7-3) induces a T cell mediated immune response against the transfected tumor cell. Optionally, a gene encoding an antisense construct which blocks expression of an MHC class II associated protein, such as the invariant chain, can also be cotransfected with a DNA encoding a peptide having the activity of a B lymphocyte antigen to promote presentation of tumor associated antigens and induce tumor specific immunity. Thus, the induction of a T cell mediated immune response in a human subject may be sufficient to overcome tumor-specific tolerance in the subject.

The activity of a protein of the invention may, among other means, be measured by the following methods:

Suitable assays for thymocyte or splenocyte cytotoxicity include, without limitation, those described in: Current Protocols in Immunology, Ed by J. E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, In Vitro assays for Mouse Lymphocyte Function 3.1-3.19; Chapter 7, Immunologic studies in Humans); Herrmann et al., Proc. Natl. Acad. Sci. USA 78:2488-2492, 1981; Herrmann et al., J. Immunol. 128:1968-1974, 1982; Handa et al., J. Immunol. 135:1564-1572, 1985; Takai et al., J. Immunol. 137:3494-3500, 1986; Takai et al., J. Immunol. 140:508-512, 1988; Herrmann et al., Proc. Natl. Acad. Sci. USA 78:2488-2492, 1981; Herrmann et al., J. Immunol. 128:1968-1974, 1982; Handa et al., J. Immunol. 135:1564-1572, 1985; Takai et al., J. Immunol. 137:3494-3500, 1986; Bowmanet al., J. Virology 61:1992-1998; Takai et al., J. Immunol. 140:508-512, 1988; Bertagnolli et al., Cellular Immunology 133:327-341, 1991; Brown et al., J. Immunol. 153:3079-3092, 1994.

Assays for T-cell-dependent immunoglobulin responses and isotype switching (which will identify, among others, proteins that modulate T-cell dependent antibody responses and that affect Th1/Th2 profiles) include, without limitation, those described in: Maliszewski, J. Immunol. 144:3028-3033, 1990; and Assays for B cell function: *In vitro* antibody production, Mond, J.J. and Brunswick, M. In *Current Protocols in Immunology*. J.E.e.a. Coligan eds. Vol 1 pp. 3.8.1-3.8.16, John Wiley and Sons, Toronto. 1994.

Mixed lymphocyte reaction (MLR) assays (which will identify, among others, proteins that generate predominantly Th1 and CTL responses) include, without limitation, those described in: Current Protocols in Immunology, Ed by J. E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, In Vitro assays for Mouse Lymphocyte Function 3.1-3.19; Chapter 7, Immunologic studies in Humans); Takai et al., J. Immunol. 137:3494-3500, 1986; Takai et al., J. Immunol. 140:508-512, 1988; Bertagnolli et al., J. Immunol. 149:3778-3783, 1992.

Dendritic cell-dependent assays (which will identify, among others, proteins expressed by dendritic cells that activate naive T-cells) include, without limitation, those described in: Guery et al., J. Immunol. 134:536-544, 1995; Inaba et al., Journal of Experimental Medicine 173:549-559, 1991; Macatonia et al., Journal of Immunology 154:5071-5079, 1995; Porgador et al., Journal of Experimental Medicine 182:255-260, 1995; Nair et al., Journal of Virology 67:4062-4069, 1993; Huang et al., Science 264:961-965, 1994; Macatonia et al., Journal of Experimental Medicine 169:1255-1264, 1989; Bhardwaj et al., Journal of Clinical Investigation 94:797-807, 1994; and Inaba et al., Journal of Experimental Medicine 172:631-640, 1990.

Assays for lymphocyte survival/apoptosis (which will identify, among others, proteins that prevent apoptosis after superantigen induction and proteins that regulate lymphocyte homeostasis) include, without limitation, those described in: Darzynkiewicz et al., Cytometry 13:795-808, 1992; Gorczyca et al., Leukemia 7:659-670, 1993; Gorczyca et al., Cancer Research 53:1945-1951, 1993; Itoh et al., Cell 66:233-243, 1991; Zacharchuk, Journal of Immunology 145:4037-4045, 1990; Zamai et al., Cytometry 14:891-897, 1993; Gorczyca et al., International Journal of Oncology 1:639-648, 1992.

Assays for proteins that influence early steps of T-cell commitment and development include, without limitation, those described in: Antica et al., Blood 84:111-117, 1994; Fine et al., Cellular Immunology 155:111-122, 1994; Galy et al., Blood 85:2770-2778, 1995; Toki et al., Proc. Nat. Acad Sci. USA 88:7548-7551, 1991.

Hematopoiesis Regulating Activity

A protein of the present invention may be useful in regulation of hematopoiesis and, consequently, in the treatment of myeloid or lymphoid cell deficiencies. Even marginal biological activity in support of colony forming cells or of factor-dependent cell lines indicates involvement in regulating hematopoiesis, e.g. in supporting the growth and proliferation of erythroid progenitor cells alone or in combination with other cytokines, thereby indicating utility, for example, in treating various anemias or for use in conjunction with irradiation/chemotherapy to stimulate the production of erythroid precursors and/or erythroid cells; in supporting the growth and proliferation of myeloid cells such as granulocytes and monocytes/macrophages (i.e., traditional CSF activity) useful, for example, in conjunction with chemotherapy to prevent or treat consequent myelo-suppression; in supporting the growth and proliferation of megakaryocytes and consequently of platelets thereby allowing prevention or treatment of various platelet disorders such as thrombocytopenia, and generally for use in place of or complimentary to platelet transfusions; and/or in supporting the growth and proliferation of hematopoietic stem cells which are capable of maturing to any and all of the above-mentioned hematopoietic cells and therefore find therapeutic utility in various stem cell disorders (such as those usually treated with transplantation, including, without limitation, aplastic anemia and paroxysmal nocturnal hemoglobinuria), as well as in repopulating the stem cell compartment post irradiation/chemotherapy, either *in-vivo* or *ex-vivo* (i.e., in conjunction with bone marrow transplantation or with peripheral progenitor cell transplantation (homologous or heterologous)) as normal cells or genetically manipulated for gene therapy.

The activity of a protein of the invention may, among other means, be measured by the following methods:

Suitable assays for proliferation and differentiation of various hematopoietic lines are cited above.

Assays for embryonic stem cell differentiation (which will identify, among others, proteins that influence embryonic differentiation hematopoiesis) include, without limitation, those described in: Johansson et al. Cellular Biology 15:141-151, 1995; Keller et al., Molecular and Cellular Biology 13:473-486, 1993; McClanahan et al., Blood 81:2903-2915, 1993.

Assays for stem cell survival and differentiation (which will identify, among others, proteins that regulate lympho-hematopoiesis) include, without limitation, those described in: Methylcellulose colony forming assays, Freshney, M.G. In *Culture of Hematopoietic*

Cells. R.I. Freshney, *et al.* eds. Vol pp. 265-268, Wiley-Liss, Inc., New York, NY. 1994; Hirayama et al., Proc. Natl. Acad. Sci. USA 89:5907-5911, 1992; Primitive hematopoietic colony forming cells with high proliferative potential, McNiece, I.K. and Briddell, R.A. In *Culture of Hematopoietic Cells*. R.I. Freshney, *et al.* eds. Vol pp. 23-39, Wiley-Liss, Inc., New York, NY. 1994; Neben et al., Experimental Hematology 22:353-359, 1994; Cobblestone area forming cell assay, Ploemacher, R.E. In *Culture of Hematopoietic Cells*. R.I. Freshney, *et al.* eds. Vol pp. 1-21, Wiley-Liss, Inc.., New York, NY. 1994; Long term bone marrow cultures in the presence of stromal cells, Spooncer, E., Dexter, M. and Allen, T. In *Culture of Hematopoietic Cells*. R.I. Freshney, *et al.* eds. Vol pp. 163-179, Wiley-Liss, Inc., New York, NY. 1994; Long term culture initiating cell assay, Sutherland, H.J. In *Culture of Hematopoietic Cells*. R.I. Freshney, *et al.* eds. Vol pp. 139-162, Wiley-Liss, Inc., New York, NY. 1994.

Tissue Growth Activity

A protein of the present invention also may have utility in compositions used for bone, cartilage, tendon, ligament and/or nerve tissue growth or regeneration, as well as for wound healing and tissue repair and replacement, and in the treatment of burns, incisions and ulcers.

A protein of the present invention, which induces cartilage and/or bone growth in circumstances where bone is not normally formed, has application in the healing of bone fractures and cartilage damage or defects in humans and other animals. Such a preparation employing a protein of the invention may have prophylactic use in closed as well as open fracture reduction and also in the improved fixation of artificial joints. *De novo* bone formation induced by an osteogenic agent contributes to the repair of congenital, trauma induced, or oncologic resection induced craniofacial defects, and also is useful in cosmetic plastic surgery.

A protein of this invention may also be used in the treatment of periodontal disease, and in other tooth repair processes. Such agents may provide an environment to attract bone-forming cells, stimulate growth of bone-forming cells or induce differentiation of progenitors of bone-forming cells. A protein of the invention may also be useful in the treatment of osteoporosis or osteoarthritis, such as through stimulation of bone and/or cartilage repair or by blocking inflammation or processes of tissue destruction (collagenase activity, osteoclast activity, etc.) mediated by inflammatory processes.

Another category f tissue regeneration activity that may be attributable to the protein of the present invention is tendon/ligament formation. A protein of the present invention, which induces tendon/ligament-like tissue or other tissue formation in circumstances where such tissue is not normally formed, has application in the healing of tendon or ligament tears, deformities and other tendon or ligament defects in humans and other animals. Such a preparation employing a tendon/ligament-liketissue inducing protein may have prophylactic use in preventing damage to tendon or ligament tissue, as well as use in the improved fixation of tendon or ligament to bone or other tissues, and in repairing defects to tendon or ligament tissue. De novo tendon/ligament-liketissue formation induced by a composition of the present invention contributes to the repair of congenital, trauma induced, or other tendon or ligament defects of other origin, and is also useful in cosmetic plastic surgery for attachment or repair of tendons or ligaments. The compositions of the present invention may provide an environment to attract tendon- or ligament-forming cells, stimulate growth of tendon- or ligament-forming cells, induce differentiation of progenitors of tendon- or ligament-forming cells, or induce growth of tendon/ligament cells or progenitors *ex vivo* for return *in vivo* to effect tissue repair. The compositions of the invention may also be useful in the treatment of tendinitis, carpal tunnel syndrome and other tendon or ligament defects. The compositions may also include an appropriate matrix and/or sequestering agent as a carrier as is well known in the art.

The protein of the present invention may also be useful for proliferation of neural cells and for regeneration of nerve and brain tissue, *i.e.* for the treatment of central and peripheral nervous system diseases and neuropathies, as well as mechanical and traumatic disorders, which involve degeneration, death or trauma to neural cells or nerve tissue. More specifically, a protein may be used in the treatment of diseases of the peripheral nervous system, such as peripheral nerve injuries, peripheral neuropathy and localized neuropathies, and central nervous system diseases, such as Alzheimer's, Parkinson's disease, Huntington's disease, amyotrophic lateral sclerosis, and Shy-Drager syndrome. Further conditions which may be treated in accordance with the present invention include mechanical and traumatic disorders, such as spinal cord disorders, head trauma and cerebrovascular diseases such as stroke. Peripheral neuropathies resulting from chemotherapy or other medical therapies may also be treatable using a protein of the invention.

Pr teins of the invention may also be useful to promote better or faster closure of non-healing wounds, including without limitation pressure ulcers, ulcers associated with vascular insufficiency, surgical and traumatic wounds, and the like.

It is expected that a protein of the present invention may also exhibit activity for generation or regeneration of other tissues, such as organs (including, for example, pancreas, liver, intestine, kidney, skin, endothelium), muscle (smooth, skeletal or cardiac) and vascular (including vascular endothelium) tissue, or for promoting the growth of cells comprising such tissues. Part of the desired effects may be by inhibition or modulation of fibrotic scarring to allow normal tissue to regenerate. A protein of the invention may also exhibit angiogenic activity.

A protein of the present invention may also be useful for gut protection or regeneration and treatment of lung or liver fibrosis, reperfusion injury in various tissues, and conditions resulting from systemic cytokine damage.

A protein of the present invention may also be useful for promoting or inhibiting differentiation of tissues described above from precursor tissues or cells; or for inhibiting the growth of tissues described above.

The activity of a protein of the invention may, among other means, be measured by the following methods:

Assays for tissue generation activity include, without limitation, those described in: International Patent Publication No. WO95/16035 (bone, cartilage, tendon); International Patent Publication No. WO95/05846 (nerve, neuronal); International Patent Publication No. WO91/07491 (skin, endothelium).

Assays for wound healing activity include, without limitation, those described in: Winter, Epidermal Wound Healing, pps. 71-112 (Maibach, HI and Rovee, DT, eds.), Year Book Medical Publishers, Inc., Chicago, as modified by Eaglstein and Mertz, J. Invest. Dermatol 71:382-84 (1978).

Activin/Inhibin Activity

A protein of the present invention may also exhibit activin- or inhibin-related activities. Inhibins are characterized by their ability to inhibit the release of follicle stimulating hormone (FSH), while activins and are characterized by their ability to stimulate the release of follicle stimulating hormone (FSH). Thus, a protein of the present invention, alone or in heterodimers with a member of the inhibin α family, may be useful as a contraceptive based on the ability of inhibins to decrease fertility in female mammals and

decrease spermatogenesis in male mammals. Administrati nof sufficient amounts of ther inhibins can induce infertility in these mammals. Alternatively, the pr tein of the invention, as a homodimer or as a heterodimer with other protein subunits of the inhibin-β group, may be useful as a fertility inducing therapeutic, based upon the ability of activin molecules in stimulating FSH release from cells of the anterior pituitary. See, for example, United States Patent 4,798,885. A protein of the invention may also be useful for advancement of the onset of fertility in sexually immature mammals, so as to increase the lifetime reproductive performance of domestic animals such as cows, sheep and pigs.

The activity of a protein of the invention may, among other means, be measured by the following methods:

Assays for activin/inhibin activity include, without limitation, those described in: Vale et al., Endocrinology 91:562-572, 1972; Ling et al., Nature 321:779-782, 1986; Vale et al., Nature 321:776-779, 1986; Mason et al., Nature 318:659-663, 1985; Forage et al., Proc. Natl. Acad. Sci. USA 83:3091-3095, 1986.

Chemotactic/Chemokinetic Activity

A protein of the present invention may have chemotactic or chemokinetic activity (e.g., act as a chemokine) for mammalian cells, including, for example, monocytes, fibroblasts, neutrophils, T-cells, mast cells, eosinophils, epithelial and/or endothelial cells. Chemotactic and chemokinetic proteins can be used to mobilize or attract a desired cell population to a desired site of action. Chemotactic or chemokinetic proteins provide particular advantages in treatment of wounds and other trauma to tissues, as well as in treatment of localized infections. For example, attraction of lymphocytes, monocytes or neutrophils to tumors or sites of infection may result in improved immune responses against the tumor or infecting agent.

A protein or peptide has chemotactic activity for a particular cell population if it can stimulate, directly or indirectly, the directed orientation or movement of such cell population. Preferably, the protein or peptide has the ability to directly stimulate directed movement of cells. Whether a particular protein has chemotactic activity for a population of cells can be readily determined by employing such protein or peptide in any known assay for cell chemotaxis.

The activity of a protein of the invention may, among other means, be measured by the following methods:

Assays for chemotactic activity (which will identify proteins that induce or prevent chemotaxis) consist of assays that measure the ability of a protein to induce the migration of cells across a membrane as well as the ability of a protein to induce the adhesion of one cell population to another cell population. Suitable assays for movement and adhesion include, without limitation, those described in: Current Protocols in Immunology, Ed by J.E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W.Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 6.12, Measurement of alpha and beta Chemokines 6.12.1-6.12.28; Taub et al. J. Clin. Invest. 95:1370-1376, 1995; Lind et al. APMIS 103:140-146, 1995; Muller et al Eur. J. Immunol. 25: 1744-1748; Gruber et al. J. of Immunol. 152:5860-5867, 1994; Johnston et al. J. of Immunol. 153: 1762-1768, 1994.

Hemostatic and Thrombolytic Activity

A protein of the invention may also exhibit hemostatic or thrombolytic activity. As a result, such a protein is expected to be useful in treatment of various coagulation disorders (including hereditary disorders, such as hemophilias) or to enhance coagulation and other hemostatic events in treating wounds resulting from trauma, surgery or other causes. A protein of the invention may also be useful for dissolving or inhibiting formation of thromboses and for treatment and prevention of conditions resulting therefrom (such as, for example, infarction of cardiac and central nervous system vessels (e.g., stroke).

The activity of a protein of the invention may, among other means, be measured by the following methods:

Assay for hemostatic and thrombolytic activity include, without limitation, those described in: Linet et al., J. Clin. Pharmacol. 26:131-140, 1986; Burdick et al., Thrombosis Res. 45:413-419, 1987; Humphrey et al., Fibrinolysis 5:71-79 (1991); Schaub, Prostaglandins 35:467-474, 1988.

Receptor/Ligand Activity

A protein of the present invention may also demonstrate activity as receptors, receptor ligands or inhibitors or agonists of receptor/ligand interactions. Examples of such receptors and ligands include, without limitation, cytokine receptors and their ligands, receptor kinases and their ligands, receptor phosphatases and their ligands, receptors involved in cell-cell interactions and their ligands (including without limitation, cellular adhesion molecules (such as selectins, integrins and their ligands) and receptor/ligand pairs involved in antigen presentation, antigen recognition and development of cellular and

humoral immune responses). Receptors and ligands are also useful for screening of potential peptide or small molecule inhibitors of the relevant receptor/ligand interaction. A protein of the present invention (including, without limitation, fragments of receptors and ligands) may themselves be useful as inhibitors of receptor/ligand interactions.

The activity of a protein of the invention may, among other means, be measured by the following methods:

Suitable assays for receptor-ligand activity include without limitation those described in: Current Protocols in Immunology, Ed by J.E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W.Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 7.28, Measurement of Cellular Adhesion under static conditions 7.28.1-7.28.22), Takai et al., Proc. Natl. Acad. Sci. USA 84:6864-6868, 1987; Bierer et al., J. Exp. Med. 168:1145-1156, 1988; Rosenstein et al., J. Exp. Med. 169:149-160 1989; Stoltenborg et al., J. Immunol. Methods 175:59-68, 1994; Stitt et al., Cell 80:661-670, 1995.

Anti-Inflammatory Activity

Proteins of the present invention may also exhibit anti-inflammatory activity. The anti-inflammatory activity may be achieved by providing a stimulus to cells involved in the inflammatory response, by inhibiting or promoting cell-cell interactions (such as, for example, cell adhesion), by inhibiting or promoting chemotaxis of cells involved in the inflammatory process, inhibiting or promoting cell extravasation, or by stimulating or suppressing production of other factors which more directly inhibit or promote an inflammatory response. Proteins exhibiting such activities can be used to treat inflammatory conditions including chronic or acute conditions), including without limitation inflammation associated with infection (such as septic shock, sepsis or systemic inflammatory response syndrome (SIRS)), ischemia-reperfusion injury, endotoxin lethality, arthritis, complement-mediated hyperacute rejection, nephritis, cytokine or chemokine-induced lung injury, inflammatory bowel disease, Crohn's disease or resulting from over production of cytokines such as TNF or IL-1. Proteins of the invention may also be useful to treat anaphylaxis and hypersensitivity to an antigenic substance or material.

Tumor Inhibition Activity

In addition to the activities described above for immunological treatment or prevention of tumors, a protein of the invention may exhibit other anti-tumor activities. A

protein may inhibit tumor growth directly r indirectly (such as, for example, via ADCC). A protein may exhibit its tumor inhibitory activity by acting on tumor tissue or tumor precursor tissue, by inhibiting formation of tissues necessary to support tumor growth (such as, for example, by inhibiting angiogenesis), by causing production of other factors, agents or cell types which inhibit tumor growth, or by suppressing, eliminating or inhibiting factors, agents or cell types which promote tumor growth.

Other Activities

A protein of the invention may also exhibit one or more of the following additional activities or effects: inhibiting the growth, infection or function of, or killing, infectious agents, including, without limitation, bacteria, viruses, fungi and other parasites; effecting (suppressing or enhancing) bodily characteristics, including, without limitation, height, weight, hair color, eye color, skin, fat to lean ratio or other tissue pigmentation, or organ or body part size or shape (such as, for example, breast augmentation or diminution, change in bone form or shape); effecting biorhythms or caricadic cycles or rhythms; effecting the fertility of male or female subjects; effecting the metabolism, catabolism, anabolism, processing, utilization, storage or elimination of dietary fat, lipid, protein, carbohydrate, vitamins, minerals, cofactors or other nutritional factors or component(s); effecting behavioral characteristics, including, without limitation, appetite, libido, stress, cognition (including cognitive disorders), depression (including depressive disorders) and violent behaviors; providing analgesic effects or other pain reducing effects; promoting differentiation and growth of embryonic stem cells in lineages other than hematopoietic lineages; hormonal or endocrine activity; in the case of enzymes, correcting deficiencies of the enzyme and treating deficiency-related diseases; treatment of hyperproliferative disorders (such as, for example, psoriasis); immunoglobulin-like activity (such as, for example, the ability to bind antigens or complement); and the ability to act as an antigen in a vaccine composition to raise an immune response against such protein or another material or entity which is cross-reactive with such protein.

ADMINISTRATION AND DOSING

A protein of the present invention (from whatever source derived, including without limitation from recombinant and non-recombinant sources) may be used in a pharmaceutical

composition when combined with a pharmaceutically acceptable carrier. Such a composition may also contain (in addition to protein and a carrier) diluents, fillers, salts, buffers, stabilizers, solubilizers, and other materials well known in the art. The term "pharmaceutically acceptable" means a non-toxic material that does not interfere with the effectiveness of the biological activity of the active ingredient(s). The characteristics of the carrier will depend on the route of administration. The pharmaceutical composition of the invention may also contain cytokines, lymphokines, or other hematopoietic factors such as M-CSF, GM-CSF, TNF, IL-1, IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-8, IL-9, IL-10, IL-11, IL-12, IL-13, IL-14, IL-15, IFN, TNF0, TNF1, TNF2, G-CSF, Meg-CSF, thrombopoietin, stem cell factor, and erythropoietin. The pharmaceutical composition may further contain other agents which either enhance the activity of the protein or compliment its activity or use in treatment. Such additional factors and/or agents may be included in the pharmaceutical composition to produce a synergistic effect with protein of the invention, or to minimize side effects. Conversely, protein of the present invention may be included in formulations of the particular cytokine, lymphokine, other hematopoietic factor, thrombolytic or anti-thrombotic factor, or anti-inflammatory agent to minimize side effects of the cytokine, lymphokine, other hematopoietic factor, thrombolytic or anti-thrombotic factor, or anti-inflammatory agent.

A protein of the present invention may be active in multimers (e.g., heterodimers or homodimers) or complexes with itself or other proteins. As a result, pharmaceutical compositions of the invention may comprise a protein of the invention in such multimeric or complexed form.

The pharmaceutical composition of the invention may be in the form of a complex of the protein(s) of present invention along with protein or peptide antigens. The protein and/or peptide antigen will deliver a stimulatory signal to both B and T lymphocytes. B lymphocytes will respond to antigen through their surface immunoglobulin receptor. T lymphocytes will respond to antigen through the T cell receptor (TCR) following presentation of the antigen by MHC proteins. MHC and structurally related proteins including those encoded by class I and class II MHC genes on host cells will serve to present the peptide antigen(s) to T lymphocytes. The antigen components could also be supplied as purified MHC-peptide complexes alone or with co-stimulatory molecules that can directly signal T cells. Alternatively antibodies able to bind surface immunolgobulin and other molecules on B cells as well as antibodies able to bind the TCR and other

molecules on T cells can be combined with the pharmaceutical composition of the invention.

The pharmaceutical composition of the invention may be in the form of a liposome in which protein of the present invention is combined, in addition to other pharmaceutically acceptable carriers, with amphipathic agents such as lipids which exist in aggregated form as micelles, insoluble monolayers, liquid crystals, or lamellar layers in aqueous solution. Suitable lipids for liposomal formulation include, without limitation, monoglycerides, diglycerides, sulfatides, lysolecithin, phospholipids, saponin, bile acids, and the like. Preparation of such liposomal formulations is within the level of skill in the art, as disclosed, for example, in U.S. Patent No. 4,235,871; U.S. Patent No. 4,501,728; U.S. Patent No. 4,837,028; and U.S. Patent No. 4,737,323, all of which are incorporated herein by reference.

As used herein, the term "therapeutically effective amount" means the total amount of each active component of the pharmaceutical composition or method that is sufficient to show a meaningful patient benefit, i.e., treatment, healing, prevention or amelioration of the relevant medical condition, or an increase in rate of treatment, healing, prevention or amelioration of such conditions. When applied to an individual active ingredient, administered alone, the term refers to that ingredient alone. When applied to a combination, the term refers to combined amounts of the active ingredients that result in the therapeutic effect, whether administered in combination, serially or simultaneously.

In practicing the method of treatment or use of the present invention, a therapeutically effective amount of protein of the present invention is administered to a mammal having a condition to be treated. Protein of the present invention may be administered in accordance with the method of the invention either alone or in combination with other therapies such as treatments employing cytokines, lymphokines or other hematopoietic factors. When co-administered with one or more cytokines, lymphokines or other hematopoietic factors, protein of the present invention may be administered either simultaneously with the cytokine(s), lymphokine(s), other hematopoietic factor(s), thrombolytic or anti-thrombotic factors, or sequentially. If administered sequentially, the attending physician will decide on the appropriate sequence of administering protein of the present invention in combination with cytokine(s), lymphokine(s), other hematopoietic factor(s), thrombolytic or anti-thrombotic factors.

Administration of protein of the present invention used in the pharmaceutical composition or to practice the method of the present invention can be carried out in a

variety of conventional ways, such as oral ingestion, inhalation, topical application r cutaneous, subcutaneous, intraperitoneal, parenteral or intravenous injection. Intravenous administration to the patient is preferred.

When a therapeutically effective amount of protein of the present invention is administered orally, protein of the present invention will be in the form of a tablet, capsule, powder, solution or elixir. When administered in tablet form, the pharmaceutical composition of the invention may additionally contain a solid carrier such as a gelatin or an adjuvant. The tablet, capsule, and powder contain from about 5 to 95% protein of the present invention, and preferably from about 25 to 90% protein of the present invention. When administered in liquid form, a liquid carrier such as water, petroleum, oils of animal or plant origin such as peanut oil, mineral oil, soybean oil, or sesame oil, or synthetic oils may be added. The liquid form of the pharmaceutical composition may further contain physiological saline solution, dextrose or other saccharide solution, or glycols such as ethylene glycol, propylene glycol or polyethylene glycol. When administered in liquid form, the pharmaceutical composition contains from about 0.5 to 90% by weight of protein of the present invention, and preferably from about 1 to 50% protein of the present invention.

When a therapeutically effective amount of protein of the present invention is administered by intravenous, cutaneous or subcutaneous injection, protein of the present invention will be in the form of a pyrogen-free, parenterally acceptable aqueous solution. The preparation of such parenterally acceptable protein solutions, having due regard to pH, isotonicity, stability, and the like, is within the skill in the art. A preferred pharmaceutical composition for intravenous, cutaneous, or subcutaneous injection should contain, in addition to protein of the present invention, an isotonic vehicle such as Sodium Chloride Injection, Ringer's Injection, Dextrose Injection, Dextrose and Sodium Chloride Injection, Lactated Ringer's Injection, or other vehicle as known in the art. The pharmaceutical composition of the present invention may also contain stabilizers, preservatives, buffers, antioxidants, or other additives known to those of skill in the art.

The amount of protein of the present invention in the pharmaceutical composition of the present invention will depend upon the nature and severity of the condition being treated, and on the nature of prior treatments which the patient has undergone. Ultimately, the attending physician will decide the amount of protein of the present invention with which to treat each individual patient. Initially, the attending physician will administer low doses of protein of the present invention and observe the patient's response. Larger doses

of protein of the present invention may be administered until th optimal therapeutic effect is obtained f r the patient, and at that point the dosage is not increased further. It is contemplated that the various pharmaceutical compositions used to practice the method of the present invention should contain about 0.01 μg to about 100 mg (preferably about 0.1μg to about 10 mg, more preferably about 0.1 μg to about 1 mg) of protein of the present invention per kg body weight.

The duration of intravenous therapy using the pharmaceutical composition of the present invention will vary, depending on the severity of the disease being treated and the condition and potential idiosyncratic response of each individual patient. It is contemplated that the duration of each application of the protein of the present invention will be in the range of 12 to 24 hours of continuous intravenous administration. Ultimately the attending physician will decide on the appropriate duration of intravenous therapy using the pharmaceutical composition of the present invention.

Protein of the invention may also be used to immunize animals to obtain polyclonal and monoclonal antibodies which specifically react with the protein. Such antibodies may be obtained using either the entire protein or fragments thereof as an immunogen. The peptide immunogens additionally may contain a cysteine residue at the carboxyl terminus, and are conjugated to a hapten such as keyhole limpet hemocyanin (KLH). Methods for synthesizing such peptides are known in the art, for example, as in R.P. Merrifield, J. Amer.Chem.Soc. 85, 2149-2154 (1963); J.L. Krstenansky, *et al.*, FEBS Lett. 211, 10 (1987). Monoclonal antibodies binding to the protein of the invention may be useful diagnostic agents for the immunodetection of the protein. Neutralizing monoclonal antibodies binding to the protein may also be useful therapeutics for both conditions associated with the protein and also in the treatment of some forms of cancer where abnormal expression of the protein is involved. In the case of cancerous cells or leukemic cells, neutralizing monoclonal antibodies against the protein may be useful in detecting and preventing the metastatic spread of the cancerous cells, which may be mediated by the protein.

For compositions of the present invention which are useful for bone, cartilage, tendon or ligament regeneration, the therapeutic method includes administering the composition topically, systematically, or locally as an implant or device. When administered, the therapeutic composition for use in this invention is, of course, in a pyrogen-free, physiologically acceptable form. Further, the composition may desirably be encapsulated or injected in a viscous form for delivery to the site of bone, cartilage or tissue

damage. Topical administration may be suitable for wound healing and tissue repair. Therapeutically useful agents other than a protein of the invention which may also optionally be included in the composition as described above, may alternatively or additionally, be administered simultaneously or sequentially with the composition in the methods of the invention. Preferably for bone and/or cartilage formation, the composition would include a matrix capable of delivering the protein-containing composition to the site of bone and/or cartilage damage, providing a structure for the developing bone and cartilage and optimally capable of being resorbed into the body. Such matrices may be formed of materials presently in use for other implanted medical applications.

The choice of matrix material is based on biocompatibility, biodegradability, mechanical properties, cosmetic appearance and interface properties. The particular application of the compositions will define the appropriate formulation. Potential matrices for the compositions may be biodegradable and chemically defined calcium sulfate, tricalciumphosphate, hydroxyapatite, polylactic acid, polyglycolic acid and polyanhydrides. Other potential materials are biodegradable and biologically well-defined, such as bone or dermal collagen. Further matrices are comprised of pure proteins or extracellular matrix components. Other potential matrices are nonbiodegradable and chemically defined, such as sintered hydroxapatite, bioglass, aluminates, or other ceramics. Matrices may be comprised of combinations of any of the above mentioned types of material, such as polylactic acid and hydroxyapatite or collagen and tricalciumphosphate. The bioceramics may be altered in composition, such as in calcium-aluminate-phosphate and processing to alter pore size, particle size, particle shape, and biodegradability.

Presently preferred is a 50:50 (mole weight) copolymer of lactic acid and glycolic acid in the form of porous particles having diameters ranging from 150 to 800 microns. In some applications, it will be useful to utilize a sequestering agent, such as carboxymethyl cellulose or autologous blood clot, to prevent the protein compositions from disassociating from the matrix.

A preferred family of sequestering agents is cellulosic materials such as alkylcelluloses (including hydroxyalkylcelluloses), including methylcellulose, ethylcellulose, hydroxyethylcellulose, hydroxypropylcellulose, hydroxypropyl-methylcellulose, and carboxymethylcellulose, the most preferred being cationic salts of carboxymethylcellulose (CMC). Other preferred sequestering agents include hyaluronic acid, sodium alginate, poly(ethylene glycol), polyoxyethylene oxide, carboxyvinyl polymer and poly(vinyl alcohol). The amount of sequestering agent useful herein is 0.5-20 wt%, preferably 1-10

wt% based on total formulation weight, which represents the amount necessary to prevent desorbtion of the protein from the polymer matrix and t pr vide appropriate handling of the composition, yet not so much that the progenitor cells are prevented from infiltrating the matrix, thereby providing the protein the opportunity to assist the osteogenic activity of the progenitor cells.

In further compositions, proteins of the invention may be combined with other agents beneficial to the treatment of the bone and/or cartilage defect, wound, or tissue in question. These agents include various growth factors such as epidermal growth factor (EGF), platelet derived growth factor (PDGF), transforming growth factors (TGF-α and TGF-β), and insulin-like growth factor (IGF).

The therapeutic compositions are also presently valuable for veterinary applications. Particularly domestic animals and thoroughbred horses, in addition to humans, are desired patients for such treatment with proteins of the present invention.

The dosage regimen of a protein-containing pharmaceutical composition to be used in tissue regeneration will be determined by the attending physician considering various factors which modify the action of the proteins, e.g., amount of tissue weight desired to be formed, the site of damage, the condition of the damaged tissue, the size of a wound, type of damaged tissue (e.g., bone), the patient's age, sex, and diet, the severity of any infection, time of administration and other clinical factors. The dosage may vary with the type of matrix used in the reconstitution and with inclusion of other proteins in the pharmaceutical composition. For example, the addition of other known growth factors, such as IGF I (insulin like growth factor I), to the final composition, may also effect the dosage. Progress can be monitored by periodic assessment of tissue/bone growth and/or repair, for example, X-rays, histomorphometric determinations and tetracycline labeling.

Polynucleotides of the present invention can also be used for gene therapy. Such polynucleotides can be introduced either *in vivo* or *ex vivo* into cells for expression in a mammalian subject. Polynucleotides of the invention may also be administered by other known methods for introduction of nucleic acid into a cell or organism (including, without limitation, in the form of viral vectors or naked DNA).

Cells may also be cultured *ex vivo* in the presence of proteins of the present invention in order to proliferate or to produce a desired effect on or activity in such cells. Treated cells can then be introduced *in vivo* for therapeutic purposes.

Patent and literature references cited herein are incorporated by reference as if fully set forth.

SEQUENCE LISTING

(1) GENERAL INFORMATION:

(i) APPLICANT: Jacobs, Kenneth
McCoy, John
LaVallie, Edward
Racie, Lisa
Merberg, David
Treacy, Maurice
Evans, Cheryl

(ii) TITLE OF INVENTION: SECRETED PROTEINS

(iii) NUMBER OF SEQUENCES: 59

(iv) CORRESPONDENCE ADDRESS:
(A) ADDRESSEE: Genetics Institute, Inc.
(B) STREET: 87 CambridgePark Drive
(C) CITY: Cambridge
(D) STATE: MA
(E) COUNTRY: USA
(F) ZIP: 02140

(v) COMPUTER READABLE FORM:
(A) MEDIUM TYPE: Floppy disk
(B) COMPUTER: IBM PC compatible
(C) OPERATING SYSTEM: PC-DOS/MS-DOS
(D) SOFTWARE: PatentIn Release #1.0, Version #1.30

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(viii) ATTORNEY/AGENT INFORMATION:
(A) NAME: Brown, Scott A.
(B) REGISTRATION NUMBER: 32,724
(C) REFERENCE/DOCKET NUMBER: GI6001

(ix) TELECOMMUNICATION INFORMATION:
(A) TELEPHONE: (617) 498-8224
(B) TELEFAX: (617) 876-5851

(2) INFORMATION FOR SEQ ID NO:1:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 505 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:1:

GAATTCGGCA CGAGGGCGCG GGGTCCGYWA TGGCGSCGGC AGCCGAAGGC GTACTGGCGA 60

CCCGGAGTGA TGAGCCCGCC CGAGACGATG CCSCCGTGGA GACAGCTGAG GAARCAAAGG 120

AGCCTGCTGA AAGCTGACAT CACTGAGCTC TGCCGGGACA TGTTCTCCAA AATGGCCACT 180

TACCTGACTG GGGAACTGAC GGCCACCAGT GAAGACTATA AGCTCCTGGA AAATATGAAT 240

AAACTCACCA GCTTGAAGTA TYTTGAAATG AAAGATATTG CTATAAACAT TAGTAGGAAC 300

TTAAAGGACT TAAACCAGAA ATATGCTGGA CTGCAGCCTT ATYTGGATTC AGATTCAATG 360

TTCATTGGAA GAGCAGGTAG CAGCTTTTTG AGCAGGCAGC TTACAAGTTG GRTGCMTWTT 420

TCAAAAAAAN TGGAANCCCA AGTACAAGAA GNTGGAGAAG CGATGAGAAA ATTATTTTTA 480

TGGGACAGAG TTTTTTTTTT TTAAT 505

(2) INFORMATION FOR SEQ ID NO:2:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 145 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:2:

Met Ser Pro Pro Glu Thr Met Pro Pro Trp Arg Gln Leu Arg Lys Gln
1 5 10 15

Arg Ser Leu Leu Lys Ala Asp Ile Thr Glu Leu Cys Arg Asp Met Phe
20 25 30

Ser Lys Met Ala Thr Tyr Leu Thr Gly Glu Leu Thr Ala Thr Ser Glu
35 40 45

Asp Tyr Lys Leu Leu Glu Asn Met Asn Lys Leu Thr Ser Leu Lys Tyr
50 55 60

Xaa Glu Met Lys Asp Ile Ala Ile Asn Ile Ser Arg Asn Leu Lys Asp
65 70 75 80

Leu Asn Gln Lys Tyr Ala Gly Leu Gln Pro Tyr Leu Asp Ser Asp Ser
85 90 95

Met Phe Ile Gly Arg Ala Gly Ser Ser Phe Leu Ser Arg Gln Leu Thr
100 105 110

Ser Trp Xaa Xaa Xaa Ser Lys Lys Xaa Glu Xaa Gln Val Gln Glu Xaa
115 120 125

Gly Glu Ala Met Arg Lys Leu Phe Leu Trp Asp Arg Val Phe Phe Phe
130 135 140

Xaa
145

(2) INFORMATION FOR SEQ ID NO:3:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 315 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:3:

GCAGCTTATC ACCTTGTGAA TGTCGGTAAC TTACTTTTCC ATAATATTGC AAATAACATA 60

AAATNTTAAA ATAATTCCAA GCTGAGTTTT CTAGATTGAG CAGAAATGGT GAAAGGAGTA 120

TTGATAACTT GGCGTATGTG ATGGGCCCCT CTTGTTTATT TTNTATGTGA GTCACATTGA 180

CATGCGATCA GTTTGGGGAA ATGTGATGAA AACAAAGACT AGATGGGTAT GTGTGTTTAT 240

GTGTTGGGTA GGGAGGTGAC GATTGCCANT CATANAATAA AGGATTTTAT AAAATACCAA 300

AAAAAAAAAA AAAAA 315

(2) INFORMATION FOR SEQ ID NO:4:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 867 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:4:

GTCAGTNTGA GTNAGAAAAT NGAATCCATC ATCTAACAGA GANTTTCATC CAGAAACAGR 60

CCATGYTGGA GAGTCTCAGC ACAGAAAAGA ACTNCCTGGT CTTTCAACTG GAGCGCCTCG 120

AACAGCAGAT GAACTCCGCC TCTGGAAGTA GTAGTAATGG GTCTTCGATT AATATGTCTG 180

GAATTGACAA TGGTGAAGGC ACTCGTCTGC GAATGTTCCT GTTCTTTTTA ATGACACAGA 240

AACTAATCTG GCAGGAATGT ACGGAAAAGT TCGCAAAGCT GCTAGTTCAA TTGATCAGTT 300

TAGTATTCGC CTGGGNAATT TTTCTCCGAA GATACCCCAT AGCGCGAGTT TTTGTAATTA 360

TATATATGGC TTTGCTTCAC CTCTGGGTNA TGATTGTTCT GTTGACTTAC ACACCAGAAA 420

TGCACCACGA CCAACCATAT GGCAAATGAA CCAAGCCCAG TTGTTGCAGT GATTGGTTGT 480

CTTTTTYTAG ACTTGGGATY TGCAAGAAGG CCAATTGCCT AAAATTTTTG AGAACAGTGC 540

ACAAGATTAT TTTATCANTA CAAGNTTTTA AANTTTTTAA GTTATTGNAN AAGTATTTTA 600

CCTAAATTTT CCAATTTCCT TTAAATGGTA AGAGTTTTTA AAACAGACAA TAATTTAACA 660

AGNTCAGNTT TGCTTTATTT GAGTTTAGTG GTCCTAATAT ATATGTAGAG AAAGATGGTG 720

GGGTTGTTCA CCTCTGTACA GGACCTTTTG TATGTTAGGN GACATTGATT ATGGGTTATA 780

ATCAGGGAAA CTAATTGTAT TTAGTGACAA AAATAAAAAG NTTTTTTTTT TATNAAAAAA 840

AAAAAAAAAA AAAAAAAAAA AATTATT 867

(2) INFORMATION FOR SEQ ID NO:5:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 212 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:5:

Met Thr Gln Lys Leu Ile Trp Gln Glu Cys Thr Glu Lys Phe Ala Lys
1 5 10 15

Leu Leu Val Gln Leu Ile Ser Leu Val Phe Ala Trp Xaa Ile Phe Leu
20 25 30

Arg Arg Tyr Pro Ile Ala Arg Val Phe Val Ile Ile Tyr Met Ala Leu
35 40 45

Leu His Leu Trp Val Met Ile Val Leu Leu Thr Tyr Thr Pro Glu Met
50 55 60

His His Asp Gln Pro Tyr Gly Lys Xaa Thr Lys Pro Ser Cys Cys Ser
65 70 75 80

Asp Trp Leu Ser Phe Xaa Arg Leu Gly Ile Cys Lys Lys Ala Asn Cys
85 90 95

Leu Lys Phe Leu Arg Thr Val His Lys Ile Ile Leu Ser Xaa Gln Xaa
100 105 110

Phe Lys Xaa Phe Lys Leu Leu Xaa Lys Tyr Phe Thr Xaa Ile Phe Gln
115 120 125

Phe Pro Leu Asn Gly Lys Ser Phe Xaa Asn Arg Gln Xaa Phe Asn Lys
130 135 140

Xaa Xaa Phe Ala Leu Phe Glu Phe Ser Gly Pro Asn Ile Tyr Val Glu
145 150 155 160

Lys Asp Gly Gly Val Val His Leu Cys Thr Gly Pro Phe Val Cys Xaa
165 170 175

Xaa Thr Leu Ile Met Gly Tyr Asn Gln Gly Asn

(2) INFORMATION FOR SEQ ID NO:6:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 491 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:6:

CAGGATATTA GAAATGGCTA CTCCCCAGTC AATTTTCATC TTTGCAATCT GCATTTTAAT 60

GATAACAGAA TTAATTCTGG CCTCAAAAAG CTACTATGAT ATCTTAGGTG TGCCAAAATC 120

GGCATCAGAG CGCCAAATCA AGAAGGCCTT TCACAAGTTG GCCATGAAGT ACCACCCTGA 180

CAAAAATAAG AGCCCGGATG CTGAAGCAAA ATTCAGAGAG ATTGCAGAAG CATATGAAAC 240

ACTCTCAGAT GCTAATAGNA CGAAAAGAGT ATGATACACT TGGACACAGT GCTTTTACTA 300

GTGGGTAAAG GGACAARGRR GTAGTTGGRA GTTCTTTTGA GYRNKCNKTT MNYTTYAAYT 360

TTSATGACTT ATTTAAAGAC TTTGGCTTTT TTGGTYNARR CYAAAACAYT GGAKCYAANA 420

AYKTTTTGRR RWYCAWWYCC NNACACCCNN NWKGGTKSYC CAGGNGGCGT TTTTTTGNAA 480

TTCCTTTTCC C 491

(2) INFORMATION FOR SEQ ID NO:7:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 159 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:7:

Met Ala Thr Pro Gln Ser Ile Phe Ile Phe Ala Ile Cys Ile Leu Met
1 5 10 15

Ile Thr Glu Leu Ile Leu Ala Ser Lys Ser Tyr Tyr Asp Ile Leu Gly
20 25 30

Val Pro Lys Ser Ala Ser Glu Arg Gln Ile Lys Lys Ala Phe His Lys
35 40 45

Leu Ala Met Lys Tyr His Pro Asp Lys Asn Lys Ser Pro Asp Ala Glu
50 55 60

Ala Lys Phe Arg Glu Ile Ala Glu Ala Tyr Glu Thr Leu Ser Asp Ala
65 70 75 80

Asn Xaa Thr Lys Arg Val Xaa Tyr Thr Trp Thr Gln Cys Phe Tyr Xaa

85 90 95

Trp Val Lys Gly Gln Xaa Xaa Ser Trp Xaa Phe Phe Xaa Xaa Xaa Xaa
100 105 110

Xaa Xaa Xaa Xaa Xaa Xaa Leu Ile Xaa Arg Leu Trp Leu Phe Trp Xaa
115 120 125

Xaa Xaa Lys His Trp Xaa Xaa Xaa Xaa Phe Xaa Xaa Xaa Xaa Xaa Thr
130 135 140

Pro Xaa Xaa Val Xaa Gln Xaa Ala Phe Phe Xaa Asn Ser Phe Ser
145 150 155

(2) INFORMATION FOR SEQ ID NO:8:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 242 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:8:

CTTAATCTAG AGATTGACTG ANACCTCATT CTGTTNGTAA AACCAGCCAG TAATTTCTGT 60

GCAACCTTAC TATGTGCAAT ATTTTTAAAT CCTGAGAAAT GTGTGCTTTT GTTTTCGGAT 120

AGACTTATTT CTTTAGTTCT GCACTTTTCC ACATTATACT CCATATGAGT ATTAATCCTA 180

TGGATAACAT ATTAAAACAA GTGTCTCATA AAAAAAAAAA AAAAAAAATT NCCTGCGGCC 240

GC 242

(2) INFORMATION FOR SEQ ID NO:9:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 607 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:9:

GAATTCNCNG CCCTACAGCA CGGCCCTGCC CCAAGGACTT TTGNTGTCCT TGGCCAGTTT 60

CTGGTGCTAA AGAAAAGATN RAARACCTCT TCCGGGAATG GCTGAAAGAC ACTTGTGGCG 120

CCAACGCCAA GCAGTCCCGG GACTGCTTCG GATGCCTTCG AGAGTGGTGC GACGCCTTCT 180

KGTGATGCTC TCTGGGAARC TCTCAATCCC CAGCCCTCAT CCAGAGTTTG CAGCCGAGTA 240

GGGACTCNTC CCCTGTCHTT TACGAAGGAA AAGATTGCTA TTGTCGTACT CACNTCNGAC 300

GTANTCCGGG GTNTTTTGGG AGTTTTCTCC CCTAACCATT TCAACTTTTT TTGGATTHTC 360

GNTCTTGCAT GCCTCCCCCG TCCTTTTTCC CTTGCCAGTT CCCTGGTGAA CAGTTTACCA 420

GCTTTTCCTG AATGGATTNC CGGSCCCCAT CCCTCACCCC CACCYTCAAT TTCAATTCCG 480

TTTTGATAMC ATTKGGYTCC TTTTTTTGGC AGAACAGTCA MTGTCCTTGT AAAGTTTTTT 540

AGATCAATAA AGTCAGTGGC TTTCAAAAAN GNAAAAAAAA AAAAAAAAAA AAAAAAAGGG 600

CGGCCGC 607

(2) INFORMATION FOR SEQ ID NO:10:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 202 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:10:

Glu Phe Xaa Ala Leu Gln His Gly Pro Ala Pro Arg Thr Phe Xaa Val
1 5 10 15

Leu Gly Gln Phe Leu Val Leu Lys Lys Arg Xaa Lys Thr Ser Ser Gly
20 25 30

Asn Gly Xaa Lys Thr Leu Val Ala Pro Thr Pro Ser Ser Pro Gly Thr
35 40 45

Ala Ser Asp Ala Phe Glu Ser Gly Ala Thr Pro Ser Xaa Asp Ala Leu
50 55 60

Trp Glu Xaa Leu Asn Pro Gln Pro Ser Ser Arg Val Cys Ser Arg Val
65 70 75 80

Gly Thr Xaa Pro Leu Ser Phe Thr Lys Glu Lys Ile Ala Ile Val Val
85 90 95

Leu Thr Ser Asp Val Xaa Arg Gly Xaa Leu Gly Val Phe Ser Pro Asn
100 105 110

His Phe Asn Phe Phe Trp Ile Xaa Xaa Leu Ala Cys Leu Pro Arg Pro
115 120 125

Phe Ser Leu Ala Ser Ser Leu Val Asn Ser Leu Pro Ala Phe Pro Glu
130 135 140

Trp Ile

(2) INFORMATION FOR SEQ ID NO:11:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 462 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:11:

AGCTTGGAAR AARRATGAAA TTCCTTATCT TCGCATTTTT CGGTGGTGTT CACCTTTTAT 60

CCCTGTGCTC TGGGAAAGCT ATATGCAAGA ATGGCATCTC TAAGAGGACT TTTGAAGAAA 120

TAAAAGAAGA AATAGCCAGC TGTGGAGATG TTGCTAAAGC AATCATCAAC CTAGCTGTTT 180

ATGGTAAAGC CCAGAACAGA TCCTATGAGC GATTGGCACT TCTGGTTGAT ACTGTTGGAC 240

CCAGACTGAG TGGCTCCAAG AACCTAGRAA AAAGCCATCC AAATTATGTA CCAAAACCTG 300

GCAGGCAAGA TGGGGCTGGG AGGAAAGTTC ACCTGGGGAG CCAGTGAGGA ATACCCCACT 360

GGGGAGGAGG GGGGAGAAGG ATNCAGCTGT TGATNGCTGG GAGCCCAAGG ATTTCATTAA 420

GGTTAGGCCN TCCTGGGGTC TTTTGGCCAG CCAGCNTTTG GG 462

(2) INFORMATION FOR SEQ ID NO:12:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 149 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:12:

Met Lys Phe Leu Ile Phe Ala Phe Phe Gly Gly Val His Leu Leu Ser
1 5 10 15

Leu Cys Ser Gly Lys Ala Ile Cys Lys Asn Gly Ile Ser Lys Arg Thr
20 25 30

Phe Glu Glu Ile Lys Glu Glu Ile Ala Ser Cys Gly Asp Val Ala Lys
35 40 45

Ala Ile Ile Asn Leu Ala Val Tyr Gly Lys Ala Gln Asn Arg Ser Tyr
50 55 60

Glu Arg Leu Ala Leu Leu Val Asp Thr Val Gly Pro Arg Leu Ser Gly
65 70 75 80

Ser Lys Asn Leu Xaa Lys Ser His Pro Asn Tyr Val Pro Lys Pro Gly
85 90 95

Arg Gln Asp Gly Ala Gly Arg Lys Val His Leu Gly Ser Gln Xaa Gly

100 105 110

Ile Pro His Trp Gly Gly Gly Gly Arg Arg Xaa Gln Leu Leu Xaa Ala
115 120 125

Gly Ser Pro Arg Ile Ser Leu Arg Leu Gly Xaa Pro Gly Val Phe Trp
130 135 140

Pro Ala Ser Xaa Trp
145

(2) INFORMATION FOR SEQ ID NO:13:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 360 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:13:

AGAAACAGTA AGAAAGAAAC GTTTTCATGN TTCTGGCCAG GAATCCTGGG TCTGCAACTT 60

NGGAAAACTC NTCTTCACAT AACAATTTCA TCCAATTCAT NTTCAAAGCA CAACTNTATT 120

TCATGCTTTC TGNNANNATA TTTCTTGATA CTTTCCAAAT TCTCTGATTC TAGAAAAAGG 180

AATCATTNTC CCCTCCCTCC CACCACATAG AATCAACATA TGGTAGGGAT TACAGTGGGG 240

GCATTTCTTT ATATCACCTC TTAAAAACAT TGTTTCCACT TTAAAAGTAA ACACTTAATA 300

AATTTTTGGA AGATCTCTGA AAAAAAAAAA AAAAAAAAAA AAAAATTNCC TGCGGCCGCA 360

(2) INFORMATION FOR SEQ ID NO:14:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 519 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:14:

AAGCTTGGCA CGAGGGGACC CGGCGCTCTC CCCGTGTCCT CTCCACGACT CGCTCGGCCC 60

CTCTGGAATA AAACACCCGC GAGCCCCGAG GGCCCAGAGG AGGCCGACGT GCCCGAGCTC 120

CTCCGGGGGT CCCGCCCGCG AGCTTTCTTC TCGCCTTCGC ATCTCCTCCT CGCGCGTCTT 180

GGACATGCCA GGAATAAAAA GGATACTCAC TGTTACCATT CTGGCTCTCT GTCTTCCAAG 240

CCCTGGGAAT GCACAGGCAC AGTGCACGAA TGGCTTTGAC CTGGATCGCC AGTCAGGACA 300

GTGTTTAGAT ATTGATGAAT GCCGAACCAT CCCCGAGGCC TGCCGAGGAG ACATGATGTG 360

TGTTAACCAA AATGGCGGGT ATTTATGCAT TCCCCGGACA AACCCTGTGT ATCGAGGGCC 420

NTACTCGAAC CCCTACTCGA CCCCTTAYTC AGGTCCGTAA CCCAGCAGYT GGCCCCACCA 480

YTTTACAGYT CCAAAYTTTC CAAKGTTTTT CAGGGTTTT 519

(2) INFORMATION FOR SEQ ID NO:15:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 111 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:15:

Met Pro Gly Ile Lys Arg Ile Leu Thr Val Thr Ile Leu Ala Leu Cys
1 5 10 15

Leu Pro Ser Pro Gly Asn Ala Gln Ala Gln Cys Thr Asn Gly Phe Asp
20 25 30

Leu Asp Arg Gln Ser Gly Gln Cys Leu Asp Ile Asp Glu Cys Arg Thr
35 40 45

Ile Pro Glu Ala Cys Arg Gly Asp Met Met Cys Val Asn Gln Asn Gly
50 55 60

Gly Tyr Leu Cys Ile Pro Arg Thr Asn Pro Val Tyr Arg Gly Pro Tyr
65 70 75 80

Ser Asn Pro Tyr Ser Thr Pro Tyr Ser Gly Pro Xaa Pro Ser Ser Trp
85 90 95

Pro His His Phe Thr Xaa Pro Asn Phe Pro Xaa Phe Phe Arg Val
100 105 110

(2) INFORMATION FOR SEQ ID NO:16:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 54 base pairs

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 536 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:17:

GTGGAATTTG TGGGTAGTGT GATNTTTGTT TGTATCCTTT TAAGTACTGT TGATCAGTTG 60

NGACACTTAC TGGTTAAACT TACGTTGCTA AAGATTTCTC TATAATAAGC CACACATTAT 120

ATTTAGACTA TATTAAGGGA CCTTGGTTTT CTTCTAGATA GCAGCTGTCC CAAAGAAAAT 180

ATTTCTTCTT TGTCTGTTAA GATTTAGCTA TTATCTGCCA GTTGTTAAGA GGTTTTGGTT 240

CCAAACTCAA CCAGCAATGT TGAGAGCTGA ACTTAAGATA GCTGTTGTAC TTTTTGCTTT 300

CCATCTGTTA CTGTCCTTCA TTCTTGGCTC CCTACTATCT ATAAACAGCT GCTGTGAAGG 360

AAGGAAAAGT TGAATAAGGA GTTGGGCTTA AATTTTAAAA AAGGAAAAAR GAAAATTGAG 420

GTTTTAGGRT TTTCATGGGT AACAAGCTCT GGGTATTARG CTAAGGCTGG GCAAGTTTCA 480

GGWTACTAAA ATATTATTTG ATCATATCTT GGATCCNTAT YYTGRRAAAT TTAAAA 536

(2) INFORMATION FOR SEQ ID NO:18:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 93 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:18:

Met Leu Arg Ala Glu Leu Lys Ile Ala Val Val Leu Phe Ala Phe His
1 5 10 15

Leu Leu Leu Ser Phe Ile Leu Gly Ser Leu Leu Ser Ile Asn Ser Cys
20 25 30

Cys Glu Gly Arg Lys Ser Xaa Ile Arg Ser Trp Ala Xaa Ile Leu Lys
35 40 45

Lys Glu Lys Xaa Lys Leu Arg Phe Xaa Xaa Phe His Gly Xaa Gln Ala
50 55 60

Leu Gly Ile Xaa Leu Arg Leu Gly Lys Phe Gln Xaa Thr Lys Ile Leu
65 70 75 80

Phe Asp His Ile Leu Asp Pro Tyr Xaa Xaa Lys Phe Lys

85 90

(2) INFORMATION FOR SEQ ID NO:19:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 397 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:19:

AAGGTAAATT AGAAATAAGT ATGAATATTA ATAAAATAGC ATTTATCTTA TTTCTCTATT 60

TTATGTTGTG ACTTAACCTA ATTTTATTTT TTTAACATTT TCTTATTTCT TATAATATGA 120

ATGCTGATAT TTAAAGGTAG ATCTATGTGG TATTCTTTGT GTTTCTNAAT TGTATAGCTC 180

TTAAGATTAT TTGTGATCTG GATTTATGTA TTTGTTAGAT ACATACGAAT TGTTAAAATG 240

GAATGCAAGT TTTTCAAAAG CCCAGGTCTA AATGTAATGG TTGGTTTATT GTTCTATAAC 300

CCCAGCCCAT CATTTTCTGT GTAAATCATA AACAATAAAC AGAATATACT CGGTGGTCAT 360

TTCTAAAAAA AAAAAAAAAA AAATTNCCTG CGGCCGC 397

(2) INFORMATION FOR SEQ ID NO:20:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 476 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:20:

GAATTCGGCA CNAGCAGTGA AGCGCAGTGA CAGCAGTGGG AACCGGAATA TCCAAAGAGT 60

GGTTTGAAGG AGAAAGAAGC ATTGTGGCTT TATATCCTCT GGGCCTGGGT TTCCTGAAGT 120

CACCACACAT AGAGGAGAGA GAAAATGGCT GAGTTAAAGT ACATTTCTGG ATTTGGGAAT 180

GAGTGTTCTT CAGAGGATCC TCGCTGCCCA GGTTCCCTGC CAGAAGGACA GAATAATCCT 240

CAGGTCTGCC CCTACAATCT CTATGCTGAG CAGCTCTCAG GATCGGCTTT CACTTGTCCA 300

CGGAGCACCA ATAANGAGAA GCTGGCTGTA TAGGATTCTA CCTTCAGTTT YTCACAAGCC 360

CTTTGGAATC CATTTGACGA NGGCCAYGTT CACTCACAAC TGGGGNATGG AAGTTGATCC 420

TGATCCTAAC CAGNTTAGAT GGNAAACCAT TTTTGAGGTT TCCAAAAGGC ATNTTC 476

(2) INFORMATION FOR SEQ ID NO:21:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 99 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:21:

Met Ser Val Leu Gln Arg Ile Leu Ala Ala Gln Val Pro Cys Gln Lys
1 5 10 15

Asp Arg Ile Ile Leu Arg Ser Ala Pro Thr Ile Ser Met Leu Ser Ser
20 25 30

Ser Gln Asp Arg Leu Ser Leu Val His Gly Ala Pro Ile Xaa Arg Ser
35 40 45

Trp Leu Tyr Arg Ile Leu Pro Ser Val Xaa His Lys Pro Phe Gly Ile
50 55 60

His Leu Thr Xaa Ala Xaa Phe Thr His Asn Trp Gly Met Glu Val Asp
65 70 75 80

Pro Asp Pro Asn Gln Xaa Arg Trp Xaa Thr Ile Phe Glu Val Ser Lys
85 90 95

Arg His Xaa

(2) INFORMATION FOR SEQ ID NO:22:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 49 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:22:

GGGGAAAAAA AAAAAAAAAA AAAAAAAAAA AAAAAAAAAA AAACTCGAG 49

(2) INFORMATION FOR SEQ ID NO:23:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 612 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:23:

AAGCTTGGCA CGAGGCAGGG AAGGTCCTGA CCCCANCGAG CACTTCTGAC AATGAGACCA 60

GAGACTCCWC AATTATTGAT CCAGGAACTG AGCAAGATCT TCCTTCCCCT GAAAATAGTT 120

CTGTTAAAGA ATACCGAATG GAAGTTCCAT CTTCGTTTTC AGAAGACATG TCAAATATCA 180

GGTCACAGCA TGCAGAAGAA CAGTCCAACA ATGGTAGATA TGACGATTGT AAAGAATTTA 240

AAGACCTCCA CTGTTCCAAG GATTMTACCC TAGCCGAGGA AGAATCTGAG TTCCCTTCTA 300

CTTCTATCTC TGCAGTTCTG TCTGACTTAG CTGACTTGAG AAGCTGTGAT GGCCAAGCTT 360

TGCCCTCCCA GGGACCCTGA GGTTGCTTTA TCTCTCAGTT GTGGCCATTC CAGAGGACTC 420

TTTAGTCATA TGCAGCAACA TGACATTTTA GGATACCCTG TGTTAGGGAC CATTGAATCT 480

ACAATCCATG TTCGTTCACA AGGGATATCT GGGCAAAGGG AAACCAAGCT GCTTCTTTGA 540

ACATTAGGGN GTTAGGCATT GTCTTACTTT TTAAAGTCCC TCACCCCCAA CCCCCATGCT 600

GTTTTGTATA AG 612

(2) INFORMATION FOR SEQ ID NO:24:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 131 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:24:

Met Thr Ile Val Lys Asn Leu Lys Thr Ser Thr Val Pro Arg Ile Xaa
1 5 10 15

Pro Xaa Pro Arg Lys Asn Leu Ser Ser Leu Leu Leu Leu Ser Leu Gln
20 25 30

Phe Cys Leu Thr Xaa Leu Thr Xaa Glu Ala Val Met Ala Lys Leu Cys
35 40 45

Pro Pro Arg Asp Pro Glu Val Ala Leu Ser Leu Ser Cys Gly His Ser
50 55 60

Arg Gly Leu Phe Ser His Met Gln Gln His Asp Ile Leu Gly Tyr Pro
65 70 75 80

Val Leu Gly Thr Ile Glu Ser Thr Ile His Val Arg Ser Gln Gly Ile
85 90 95

Ser Gly Gln Arg Glu Thr Lys Leu Leu Leu Xaa Thr Leu Gly Xaa Xaa
100 105 110

Ala Leu Ser Tyr Phe Leu Lys Ser Leu Thr Pro Asn Pro His Ala Val
115 120 125

Leu Tyr Lys
130

(2) INFORMATION FOR SEQ ID NO:25:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 69 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:25:

TTTTTAAAAA AAAAAAAAAA AAAAAAAAAA AAAAAAAAAA AAAAAAAAAA AAATTNTCNC 60

TGCGGCCGC 69

(2) INFORMATION FOR SEQ ID NO:26:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 655 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:26:

CAATNATAAA ATGTCAGCTT TTAAGGNANN CCTGTGGAAT ATATTTTCCA GCAATAAAAA 60

GAGATCCAGG CAGATATTTA CATAGTTGTC CCTGAATCTG TGAAAAAATG GCTTCGACAG 120

CTAAAGAATG CTGGGAAAAT TCTTCTGTTA ATNACCAGTT CTCACAGTGA TTACTGTAGA 180

CTTCTCTGCG AATATATTCT TGGGAATGAT TTTACAGACC TTTTTGACAT TGTGATTACA 240

AATGCATTGA AGCCTGGTTT CTTCTCCCAC TTACCAAGTC AGAGACCTTT CCGGACACTC 300

GAGAATGATG AGGAGCAGGA GGCACTGCCA TCTCTGGATA AACCTGGCTG GTACTCCCAA 360

GGGAACGCTG TCCACCTCTA TGAACTTCTG AAGAAAATGA CTGGCAAACC TGAACCCAAG 420

GTTSTTTATT NWTGGTGWCA GCATGCAWTC AGATATTTTC CCAGCTCGTC ACTATAGTAA 480

TTGGGGAGAC AGTCCTCATC CGKGGAAGGA ACTCAGAGGG GGATGAARGG GCACGAGGGA 540

GTTCAGAGGC CTTGAGGGAG TTCAGAGCCT CTTAGAAGAA GGAAAGGGAA ATTTTGAGGG 600

GACCAAAAGN CAAAACCTTT AATTATTTCA TTTTAAANAT GGGGGTTTTT TTTTN 655

(2) INFORMATION FOR SEQ ID NO:27:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 199 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:27:

Lys Glu Ile Gln Ala Asp Ile Tyr Ile Val Val Pro Glu Ser Val Lys
1 5 10 15

Lys Trp Leu Arg Gln Leu Lys Asn Ala Gly Lys Ile Leu Leu Leu Xaa
20 25 30

Thr Ser Ser His Ser Asp Tyr Cys Arg Leu Leu Cys Glu Tyr Ile Leu
35 40 45

Gly Asn Asp Phe Thr Asp Leu Phe Asp Ile Val Ile Thr Asn Ala Leu
50 55 60

Lys Pro Gly Phe Phe Ser His Leu Pro Ser Gln Arg Pro Phe Arg Thr
65 70 75 80

Leu Glu Asn Asp Glu Glu Gln Glu Ala Leu Pro Ser Leu Asp Lys Pro
85 90 95

Gly Trp Tyr Ser Gln Gly Asn Ala Val His Leu Tyr Glu Leu Leu Lys
100 105 110

Lys Met Thr Gly Lys Pro Glu Pro Lys Val Xaa Tyr Xaa Trp Xaa Gln
115 120 125

His Ala Xaa Arg Tyr Phe Pro Ser Ser Ser Leu Xaa Xaa Leu Gly Arg
130 135 140

Gln Ser Ser Ser Xaa Glu Gly Thr Gln Arg Gly Met Lys Gly His Glu
145 150 155 160

Gly Val Gln Arg Pro Xaa Gly Ser Ser Glu Pro Leu Arg Arg Arg Lys
165 170 175

Gly Lys Phe Xaa Gly Asp Gln Lys Xaa Lys Pro Leu Ile Ile Ser Phe
180 185 190

Xaa Xaa Trp Gly Phe Phe Phe
195

(2) INFORMATION FOR SEQ ID NO:28:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 279 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:28:

TCCTCCACTG NTCTTATCAA GTGATGAGAC ACTGATATCC AAATAANTNG TATTTACTGA 60

AAAATGAAGT GAAGACCCAT ATATGCAGTT AAAAAAAAGT TAATTTTCAA AAAATACTGT 120

AAAAGACTTT AAGGAACAAG TTTTATTGAC CAATAAGTTG ATATTTGTCC ATAGGTCTCC 180

TTTCTATAAA TCATCTTGAT GTTTAACAAC TCTTATTATA TTAAAATCTC AGTATCCTAA 240

AACTTAAAAA AAAAAAAAAA AAAAACATGT TTAATTAAK 279

(2) INFORMATION FOR SEQ ID NO:29:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 391 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:29:

GAACNTGGGC CGCATGTATN TCTTCTATGG CAACAAGACC TCGGTGCAGT TCCAGAATTT 60

CTCACCCACT GTGGTTCACC CGGGAGACCT CCAGACTCAG CTGGCTGTGC AGACCAAGCG 120

CGTGGCGGCG CAGGTGGACG GCGGCGCGCA GGTGCAGCAG GTGCTCAATA TCGAGTGCCT 180

GCGGGACTTC CTGACGCCCC CGCTGCTGTC CGTGCGCTTC CGGTACGGTG GCGCCCCCCA 240

GGCCCTCACC CTGAAGCTCC CAGTGACCAT CAACAAGTTC TTCCAGCCCA CCGAGATGGC 300

GGCCCAGGAT TTCTTCCAGC GCTGGAAGCA GCTGANCCTC CCTCAACAGG AGGCGCAGAA 360

AATCTTCAAA GCCAACCACC CCATGGACGC A 391

(2) INFORMATION FOR SEQ ID NO:30:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 126 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:30:

Met Tyr Xaa Phe Tyr Gly Asn Lys Thr Ser Val Gln Phe Gln Asn Phe
1 5 10 15

Ser Pro Thr Val Val His Pro Gly Asp Leu Gln Thr Gln Leu Ala Val

```
                20                  25                  30

Gln Thr Lys Arg Val Ala Ala Gln Val Asp Gly Gly Ala Gln Val Gln
        35                  40                  45

Gln Val Leu Asn Ile Glu Cys Leu Arg Asp Phe Leu Thr Pro Pro Leu
    50                  55                  60

Leu Ser Val Arg Phe Arg Tyr Gly Gly Ala Pro Gln Ala Leu Thr Leu
65                  70                  75                  80

Lys Leu Pro Val Thr Ile Asn Lys Phe Phe Gln Pro Thr Glu Met Ala
                85                  90                  95

Ala Gln Asp Phe Phe Gln Arg Trp Lys Gln Leu Xaa Leu Pro Gln Gln
            100                 105                 110

Glu Ala Gln Lys Ile Phe Lys Ala Asn His Pro Met Asp Ala
        115                 120                 125
```

(2) INFORMATION FOR SEQ ID NO:31:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 197 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:31:

```
CCCCTCNTCC NTTTCCCCCC CAAGCACAGA GGGGAGAGGG GCCAGGGAAG TGGATGTTTC     60

TTCCCNTCCC ACCCCACCCT GTTGTAGCCC CTCCTACCCC CTCCCCATCC AGGGGCTGTG    120

TATTATTGTG AGCGNATAAA CAGAGAGACG CTAAAAAAAA AAAAAAAAAA AAAAAAATCC    180

NNTAATTAAG CGGCCGC                                                   197
```

(2) INFORMATION FOR SEQ ID NO:32:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 514 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:32:

```
AAGCTTGGCA CGTGGCTGAT TGGAGCTGTA AAACATCATC AGGTGTTGCT ATTWTTTTAT     60

ATGATTATTC TGTTACTTGT ATTTATTGTT CAGTTTTCTG TATCTTGCGC TTGTTTAGCC    120

CTGAACCAGG AGCAACAGGG TCAGCTTCTG GAGGTTGGTT GGAACAATAC GGCAAGTGCT    180
```

CGAAATGACA TCCAGAGAAA TCTAAACTGC TGTGGGTTCC GAAGTGTTAA CCCAAATGAC 240

ACCTGTCTGG CTAGCTGTGT TAAAAGTGAC CACTCGTGCT CGCCATGTGC TCCAATCATA 300

GGAGAATATG CTGGAGAGGT TTTGAGATTT GTTGGTGGCA TTGGCCTGTT CTTCAGTTTT 360

ACAGAGATCC TGGGGTGTTT GGCTGACCTA CAGATACAGG AACCAGAAAG ACCCCCGCGC 420

GAATCCTAGT GCATTCCTTT GGATGAGGAA AACAAGGGAA GNTTCCNTTT CGTATTATGG 480

NCTTGTTTCA CTTTCTGTAA TTTTTCTGTT AAGG 514

(2) INFORMATION FOR SEQ ID NO:33:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 151 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:33:

Met Ile Ile Leu Leu Leu Val Phe Ile Val Gln Phe Ser Val Ser Cys
1 5 10 15

Ala Cys Leu Ala Leu Asn Gln Glu Gln Gln Gly Gln Leu Leu Glu Val
20 25 30

Gly Trp Asn Asn Thr Ala Ser Ala Arg Asn Asp Ile Gln Arg Asn Leu
35 40 45

Asn Cys Cys Gly Phe Arg Ser Val Asn Pro Asn Asp Thr Cys Leu Ala
50 55 60

Ser Cys Val Lys Ser Asp His Ser Cys Ser Pro Cys Ala Pro Ile Ile
65 70 75 80

Gly Glu Tyr Ala Gly Glu Val Leu Arg Phe Val Gly Gly Ile Gly Leu
85 90 95

Phe Phe Ser Phe Thr Glu Ile Leu Gly Cys Leu Ala Asp Leu Gln Ile
100 105 110

Gln Glu Pro Glu Arg Pro Pro Arg Glu Ser Xaa Cys Ile Pro Leu Asp
115 120 125

Glu Glu Asn Lys Gly Xaa Phe Xaa Phe Val Leu Trp Xaa Cys Phe Thr
130 135 140

Phe Cys Asn Phe Ser Val Lys
145 150

(2) INFORMATION FOR SEQ ID NO:34:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 218 base pairs
(B) TYPE: nucleic acid

(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:34:

ACGTAGCAAA AAGATATTTG ATTATCTTAA AAATTGTTAA ATACCGTTTT CANGAAAGTT 60

CTCAGTATTG TAACAGCAAC TTGTCAAACC TAAGCATATT TGAATNTGAT NTCCCATAAT 120

TTGAAATNGA AATCGTATGG TGTGGCTCTG TATATTCTGT TAAAAAATTA AGGGACCAGA 180

AACCTTAAAA AAAAAAAAAA AAAATTCCCT GCGGCCGC 218

(2) INFORMATION FOR SEQ ID NO:35:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 525 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:35:

CAAGATTGGC AAGATGCTTA TTTNTGNNNC CATATTTGGC TGCCTTGACC CAGTGGCAAC 60

ACTAGCTGCA GTTATGACAG AGAAGTCTCC TTTTACCACA CCAATTGGTC GAAAAGATGA 120

AGCAGATCTT GCAAAATCAG CTTTGGCCAT GGCGGATTCA GACCACCTGA CGATCTACAA 180

TGCATATCTA GGATGGAAAG AAAGCACGAC AAGAAGGAGG TTATCGTTCT GAAATCACAT 240

ACTGCCGGAG GNAACTTTCT TAATANAACA TCACTGTTAA CCCTAGAGGA TGTAAAGCAG 300

GAGTTAATAA AGTTGGTTAA GGCAGCAGGA TTTTCATCTT CCACAACTTC TACCAGCTGG 360

GAAGGAAACA GANCCTCACA GACCCTCTCA TTCCAAGAAA TTGCCCTTCT TAAANCTGTA 420

CTGGTGGCTG GACTGTATGA CAATGTNGGG AAAATAATCT ATACAAATCN NTGGATGTTA 480

CANAAAAATT GGCTTGCATT GTGGANACGG CCCAGGCNAA ACACA 525

(2) INFORMATION FOR SEQ ID NO:36:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 111 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:36:

Met Glu Arg Lys His Asp Lys Lys Glu Val Ile Val Leu Lys Ser His
1 5 10 15

Thr Ala Gly Gly Asn Phe Leu Asn Xaa Thr Ser Leu Leu Thr Leu Glu
20 25 30

Asp Val Lys Gln Glu Leu Ile Lys Leu Val Lys Ala Ala Gly Phe Ser
35 40 45

Ser Ser Thr Thr Ser Thr Ser Trp Glu Gly Asn Arg Xaa Ser Gln Thr
50 55 60

Leu Ser Phe Gln Glu Ile Ala Leu Leu Lys Xaa Val Leu Val Ala Gly
65 70 75 80

Leu Tyr Asp Asn Val Gly Lys Ile Ile Tyr Thr Asn Xaa Trp Met Leu
85 90 95

Xaa Lys Asn Trp Leu Ala Leu Trp Xaa Arg Pro Arg Xaa Asn Thr
100 105 110

(2) INFORMATION FOR SEQ ID NO:37:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 109 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:37:

ACATGTATAA TTTTNTAGTT TCCTTTTTAA TGATGATTAT TCTGAATGTA TTTGCCANTA 60

CANNTACAAT AAATTTNTTT GGTATTATGC AAAAAAAAAA AAAAAAANA 109

(2) INFORMATION FOR SEQ ID NO:38:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 825 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:38:

GAATTCGGCA CGAGTTTTTT TTTTCTGCAG TTGTGTGTAT GTGTGTTTGT GTGAAGAAAA 60

ACAGACTCTG TCCAGGTAGA AATGGTGAGG AGGGGGAAGA GAATTACATT TCCAGGGTCA 120

GAAACTTGGC AACAGTTTTC CTAKAGTGAC TCAGACACAC CACAGTAACA ACTCTCGCTG 180

CAATTTTATT TTAATTTGAG AAATAAAGAT TTCCTCCAAG CCACATGAGG ACTCTGGCAC 240

CCACCCACAA AGCAAGACCT GTATTTATAA GCCGAGGGTG CAGGGAGCTN AACTGCGGGA 300

CCCGTCAGGG CCCCGTGGAC CCATCCCCGT CCCCACCCCC CCCTCCACCG YTGGGGCCCA 360

TCAGTGTGTG TTGGGGGGGA TGCTTGGGCA GCTGGGGGGT GAGGGAGACA ACAAACCTYG 420

GGGAAYTGGG AGCCAGAGCT GCGGCCTGAC TGACGCCTTT TGATGCTCAC GGGAAATTTN 480

TGCCCAGGAT NTCAGCCCCA GGCTGGTTGT TTCTACAAAT CTCTCTCAAA TGTATTATTT 540

TGGTGACAAA AATGAAGGAG CTTTGTAAAT TTTTTTAAAA TTATGAATNC ATATCAAGTA 600

GTTGTTTACA TTTCTTGAAA AAATAGGAAC TCGGGCAGCA GAATCAGATT GGCAGAATCT 660

TTAGACTACA CAGGCAATAA TCAAGTCTGC TGTTTTGNCC TTTCGTAGTA GAAGTGGTTG 720

TAGTGTTTAG ATATCTGTTT GGTCTTGCTT CTTGTATTGC ATTTTTTTCA ATAAACAACA 780

ACAAAAAGAA AAAAAAAAAA AAAAAAAAAA AAGATCTTTA ATTAA 825

(2) INFORMATION FOR SEQ ID NO:39:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 200 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:39:

Met Arg Thr Leu Ala Pro Thr His Lys Ala Arg Pro Val Phe Ile Ser
1 5 10 15

Arg Gly Cys Arg Glu Leu Asn Cys Gly Thr Arg Gln Gly Pro Val Asp
20 25 30

Pro Ser Pro Ser Pro Pro Pro Pro Pro Pro Leu Gly Pro Ile Ser Val
35 40 45

Cys Trp Gly Gly Cys Leu Gly Ser Trp Gly Val Arg Glu Thr Thr Asn
50 55 60

Leu Gly Glu Leu Gly Ala Arg Ala Ala Ala Xaa Leu Thr Pro Phe Asp
65 70 75 80

Ala His Gly Lys Phe Xaa Pro Arg Xaa Ser Ala Pro Gly Trp Leu Phe
85 90 95

Leu Gln Ile Ser Leu Lys Cys Ile Ile Leu Val Thr Lys Met Lys Glu
100 105 110

Leu Cys Lys Phe Phe Xaa Asn Tyr Glu Xaa Ile Ser Ser Ser Cys Leu
115 120 125

His Phe Leu Lys Lys Xaa Glu Leu Gly Gln Gln Asn Gln Ile Gly Arg

```
    130                 135                 140

Ile Phe Arg Leu His Arg Gln Xaa Ser Ser Leu Leu Phe Xaa Pro Phe
145                 150                 155                 160

Val Val Glu Val Val Val Val Phe Arg Tyr Leu Phe Gly Leu Ala Ser
                165                 170                 175

Cys Ile Ala Phe Phe Ser Ile Asn Asn Asn Lys Lys Lys Lys Lys Lys
            180                 185                 190

Lys Lys Lys Lys Asp Leu Xaa Leu
        195                 200
```

(2) INFORMATION FOR SEQ ID NO:40:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 508 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:40:

```
AAGCTTGGCA CGNGGTCTGT CGCTCCCGGA AACTTGTTGG CAATGCCTAT TTTTTGGCTT     60

TCCCCCGCGT TCTCTAAACT AACTATTTAA AGGTCTGCGG TCCCSAAATG GTTTGACTAA    120

ACGTAGGATG GGACTTAAGT TGAACGGCAG ATATATTTCA CTGATCCTCG CGGTGCAAAT    180

AGCGTATCTG GTGCAGGCCG TGAGAGCAGC GGGCAAGTGC GATGCGGTCT TCAAGGGCTT    240

TTCGGACTGT TTGCTCAAGC TGGGCGAMMR CATGGGCCAA CTACCCGCAG GSCTKGGACG    300

ACAAGACGAA CATCAAGACC GTGTGCACAT ACTGGGAGGA TTTCCACAGC TGCACGGTCA    360

CAGCCCTTAC GGATTGCCAG GGAAGGGGCG AAAGATATGT GGGGATAAAC TGAGAAAAGA    420

ATCCAAAAAC CTCAACATCC AAGGGCAGCT TATTTCGAAY TYTGCGGCAN GTCAACGGNG    480

GCGGCCGGGT CCTTGTTCCC GGCTTTTT                                       508
```

(2) INFORMATION FOR SEQ ID NO:41:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 127 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:41:

Met Gly Leu Lys Leu Asn Gly Arg Tyr Ile Ser Leu Ile Leu Ala Val
1 5 10 15

Gln Ile Ala Tyr Leu Val Gln Ala Val Arg Ala Ala Gly Lys Cys Asp
20 25 30

Ala Val Phe Lys Gly Phe Ser Asp Cys Leu Leu Lys Leu Gly Xaa Xaa
35 40 45

Met Gly Gln Leu Pro Ala Gly Leu Gly Arg Gln Asp Glu His Gln Asp
50 55 60

Arg Val His Ile Leu Gly Gly Phe Pro Gln Leu His Gly His Ser Pro
65 70 75 80

Tyr Gly Leu Pro Gly Lys Gly Arg Lys Ile Cys Gly Asp Lys Leu Arg
85 90 95

Lys Glu Ser Lys Asn Leu Asn Ile Gln Gly Gln Leu Ile Ser Asn Xaa
100 105 110

Ala Ala Xaa Gln Arg Xaa Arg Pro Gly Pro Cys Ser Arg Leu Phe
115 120 125

(2) INFORMATION FOR SEQ ID NO:42:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 269 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:42:

TGGTTTTAGC TGTTACACAC ACAGTAATAC CTGAATATCC CACGGTATAG ATCACANGGG 60

GGGGATGTTA AATGTTAATC TAAAATATAG CTAAAAAAAG ATTTTGACAT AAAAGAGCCT 120

TGATTTTAAA AAAAAAAGAG AGAGAGATGT AATTTAAAAA GTTTATTATA AATTAAATTC 180

AGCNAAAAAA GATTTGCTAC AAAGTATAGA GAAGTATAAA ATAAAAGTTA TTGTTTGNAA 240

AAAAAAAAAA AAAAATTNCC TGCGGCCGC 269

(2) INFORMATION FOR SEQ ID NO:43:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 676 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:43:

GAGATTTTCA GCACCCTGCG ATATGCAAGC CGAGNTCAGC GGGTCACCAC CCGACCACAG 60

GCCCCCAAGT TTCCTGTGGC AAAGCAGCCC CAGCGTTTGG AGACAGAGAT GCTGCAGCTC 120

CAGGAGGAGA ACCGTCGCCT GCAGTTCCAG NTGGACCAAA TGGANTGCAA GGCCTCAGGG 180

TTCAGTGGAG CCCGGGTGGC CTGGGCCCAG CGGAACCTGT ACGGGATGNT ACAGGAGTTT 240

CATGNTAGAG AATGAGAGGC TCAGGAAAGA AAAGAGCCAG CTGCAGAATA GCCGAGAGCT 300

AGCCCAGAAT GAGCAGCGCA TCCTGGCCCA GCAGGTCCAT GCACTAGAGA RGCGTCTCCT 360

CTCTGCCTGC TACCATCACC AGCAGGGTCC TGGCCTGACC CCACCGTGTC CCTGCTTGAT 420

GGCCCCAGCT CCCCCTTGCC ATGCACTGCC ACCCCTCTAC TCCTGCCCCT GCTGCCACAT 480

CTGCCCACTG TGTCKAGTGC CCCTGGCCCA CTGGGYYKGC CTGSCMAGGG GAGCACCACC 540

TTGCCCCAGC CTCTCTTCTG GGGCTCTGAR GAGTCAGAAA TAGACCAGAC GTGGTTTCCT 600

GGTTCTCAGG ANGGTTTTTA GTTTNAGGAG AGGGACGGTA GAAGAACCAT TTTGTTGCAA 660

AAAGAAGGGG ACCAAG 676

(2) INFORMATION FOR SEQ ID NO:44:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 218 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:44:

Met Gln Ala Glu Xaa Ser Gly Ser Pro Pro Asp His Arg Pro Pro Ser
1 5 10 15

Phe Leu Trp Gln Ser Ser Pro Ser Val Trp Arg Gln Arg Cys Cys Ser
20 25 30

Ser Arg Arg Arg Thr Val Ala Cys Ser Ser Xaa Trp Thr Lys Trp Xaa
35 40 45

Ala Arg Pro Gln Gly Ser Val Glu Pro Gly Trp Pro Gly Pro Ser Gly
50 55 60

Thr Cys Thr Gly Xaa Tyr Arg Ser Phe Met Xaa Glu Asn Glu Arg Leu
65 70 75 80

Arg Lys Glu Lys Ser Gln Leu Gln Asn Ser Arg Glu Leu Ala Gln Asn
85 90 95

Glu Gln Arg Ile Leu Ala Gln Gln Val His Ala Leu Glu Xaa Arg Leu
100 105 110

Leu Ser Ala Cys Tyr His His Gln Gln Gly Pro Gly Leu Thr Pro Pro
115 120 125

Cys Pro Cys Leu Met Ala Pro Ala Pro Pro Cys His Ala Leu Pro Pro
130 135 140

Leu Tyr Ser Cys Pro Cys Cys His Ile Cys Pro Leu Cys Xaa Val Pro
145 150 155 160

Leu Ala His Trp Xaa Xaa Leu Xaa Arg Gly Ala Pro Pro Cys Pro Ser
165 170 175

Leu Ser Ser Gly Ala Leu Xaa Ser Gln Lys Xaa Thr Arg Arg Gly Phe
180 185 190

Leu Val Leu Arg Xaa Val Phe Ser Xaa Arg Arg Gly Thr Val Glu Glu
195 200 205

Pro Phe Cys Cys Lys Lys Lys Gly Thr Lys
210 215

(2) INFORMATION FOR SEQ ID NO:45:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 394 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:45:

TTCCAAACTT GGCCCAGAGA CTGGAGGCCT TCAGAGACCA GATTGGCAGN TCCNTGCGAN 60

GTGGCCGCAG CCAGCCACCC TGCAGTGAGG GCGCACGGAG CNCAGGCCAA GTCNTCCNTC 120

CCCATTGAAG GCCAAGTGGG AACNNANNAG AATGCTGTGT GACCTCAGAC TGGGCTCCAC 180

ACTCTTGGGC TTCAGTCTGC CCATCTGCTG AATGGAGACA GCAGCTGNTA CTCCACCTGC 240

AGCTGGGCTA GGGGCGGGGA CTGGGGGTGC TATTTAGGGG AACAAGGGGA TTTCAGGAGA 300

AACCCAGGCA GCAGGGGATG AAATACATGA ATAAAGAGAG GCATCAGCTC CAAAAAAAAA 360

AAAAAAAAAA AAAGAACTTT AATTAAGCGG CCGC 394

(2) INFORMATION FOR SEQ ID NO:46:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 479 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:46:

AAGCTTGGCA CNAGGGCCAA ACCTCTATGG ATATATAAAG GGAAGCTTGA GGAGGAATTT 60

CACAGTTACA GTGCAGAAGC AGAAGCAAAA GAATTAACCA GCTCTTCAGT CAAGCAAATC 120

CTCTACTCAC CATGCTTCCT CCTGCCATTC ATTTCTATCT CCTTCCCCTT GCATGCATCC 180

TAATGAAAAG CTGTTTGGCT TTTAAAAATG ATGCCACAGA AATCCTTTAT TCACATGTGG 240

TTAAACCTGT TCCAGCACAC CCCAGCAGCA ACAGCACGTT GAATCAAGCC AGAAATGGAG 300

GCAGGCATTT CAGTAACACT GGACTGGATC GGAACACTCG GGTTCAAGTG GGTTGCCGGG 360

AACTGCGTTC CACCAAATAC ATCTCTGGAT GGGCCAGTTG CACCAGCATT CAGCCCTCTG 420

GAAGGGAGCT GGGTGTGTGG TGGGCGAGTG CTTTGCCCNT GCCAGTGGTT CCCTAACTG 479

(2) INFORMATION FOR SEQ ID NO:47:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 116 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:47:

Met Leu Pro Pro Ala Ile His Phe Tyr Leu Leu Pro Leu Ala Cys Ile
1 5 10 15

Leu Met Lys Ser Cys Leu Ala Phe Lys Asn Asp Ala Thr Glu Ile Leu
20 25 30

Tyr Ser His Val Val Lys Pro Val Pro Ala His Pro Ser Ser Asn Ser
35 40 45

Thr Leu Asn Gln Ala Arg Asn Gly Gly Arg His Phe Ser Asn Thr Gly
50 55 60

Leu Asp Arg Asn Thr Arg Val Gln Val Gly Cys Arg Glu Leu Arg Ser
65 70 75 80

Thr Lys Tyr Ile Ser Gly Trp Ala Ser Cys Thr Ser Ile Gln Pro Ser
85 90 95

Gly Arg Glu Leu Gly Val Trp Trp Ala Ser Ala Leu Pro Xaa Pro Val
100 105 110

Val Pro Xaa Leu
115

(2) INFORMATION FOR SEQ ID NO:48:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 35 base pairs
(B) TYPE: nucleic acid

(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:48:

AAGTTTAAAA AAAAAAAAAA AAATCNCGCG GCCGC 35

(2) INFORMATION FOR SEQ ID NO:49:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 296 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:49:

ACATTTACTT AAAGGAGAAA AGTAAGGGGG TCNCAGAAAT GTCTGGGGCN ATTATAGAAA 60

ACATGAGTAC CAAGAAGCTC TGCATTGTTG GAGGGATTCT TCTGGTTTTC CCAATCGTTG 120

CCTNTCTGGT GGGAGGCTTG ATCGCTCCAG CACCCACAAC ANCAGTACCC TACACGTCAA 180

TAAAATGTGT GGATGTCCGT AAGAACCACC ATAAAACAAG ATGACTGGCT CCTTGGGGAC 240

CTAACAAGTG TTTNCAGACC CATCNNTNAG CCGAACAAAC ANCCAGCGCC AATGTA 296

(2) INFORMATION FOR SEQ ID NO:50:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 332 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:50:

GAATTCGGCA CGAGCTTGAT TGCTCCAGGG CCCACAACGG CAGTGTCCTA CATGTCGGTG 60

AAATGTGTGG ATGCCCGTAA GAACCATCAC AAGACAAAAT GGTTCGTGCC TTGGGGACCC 120

AATCATTGTG ACAAGATCCG AGACATTGAA GAGGCAATTC CAAGGGAAAT TGAAGCCAAT 180

GACATCGTGT TTTCTGTTCA CATTCCCCTC CCCCACATGG GAGATGAGTC CTTGGTTCCA 240

ATTCATGMTG TTTATCCTGG CAGCTGGGAC ATTGCCTTTC AAGCTAAACA ACCAAATCAG 300

GGGAAAATGC AGGAAGTCTC CATGGGACGT TT 332

(2) INFORMATION FOR SEQ ID NO:51:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 110 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:51:

Glu Phe Gly Thr Ser Leu Ile Ala Pro Gly Pro Thr Thr Ala Val Ser
1 5 10 15

Tyr Met Ser Val Lys Cys Val Asp Ala Arg Lys Asn His His Lys Thr
20 25 30

Lys Trp Phe Val Pro Trp Gly Pro Asn His Cys Asp Lys Ile Arg Asp
35 40 45

Ile Glu Glu Ala Ile Pro Arg Glu Ile Glu Ala Asn Asp Ile Val Phe
50 55 60

Ser Val His Ile Pro Leu Pro His Met Gly Asp Glu Ser Leu Val Pro
65 70 75 80

Ile His Xaa Val Tyr Pro Gly Ser Trp Asp Ile Ala Phe Gln Ala Lys
85 90 95

Gln Pro Asn Gln Gly Lys Met Gln Glu Val Ser Met Gly Arg
100 105 110

(2) INFORMATION FOR SEQ ID NO:52:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 327 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:52:

TCACTCCTAA TCCATGACCA CTGTTTTTTT CCTATTTATA TCACCAGGTA GCCTACTGAG 60

TTAATATTTA AGTTGTCNNT GGGTNNGTGT CCCTGTTTTG TGGCATAATA TAACTGAATT 120

TCATGNGAAG ATTTATTCCA CCAGGGGTAT TTCAGCTTTG AAACCAAATC TGTGTATCTA 180

ATACTAACCA ATCTGTTGGA TGTGGATTTT AAAAAATGTT TGCTAAACTA CCCAAGTAAG 240

ATTTACTGTA TTAAATGGCC TTCGGGTCTG AAAAGCTTTT TTAAAAAAAA AAAAAAAAAA 300

AAAAAAAAAA AAAAGATCTT TAATTAA 327

(2) INFORMATION FOR SEQ ID NO:53:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 242 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:53:

GCGAAAGGAT TTTAAGGAAC AGATCATCCA CCATGTGGCC ACTATCATTC TCCTCTGCTT 60

CTCCTGGTTT GCCAATTACG TCCGGGCAGG GACCCTCATC ATGGCTCTGC ATGACGCTTC 120

TGACTACCTG CTGGAGTCTG CCAAGATGTT TAACTACGCG GGATGGAAGA ACACCTGCAA 180

CAACCTCTTC ATTGTGTTCG CCATCGTTTT CATCATCACT CGGCTGGTTA TCATGCCTTT 240

CT 242

(2) INFORMATION FOR SEQ ID NO:54:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 377 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:54:

GAATTCGGCA CGAGGATTCT CATCAGCTTT TCCTGGGTTT GCCAATTACA TCCGAGCTGG 60

GACTCTAATC ATGGCTCTGC ATGACTCTTC CGATTACCTG CTGGAKTCAG CCAAGATGTT 120

TAACTACGCG GGATGGAAGA ACACCTGCAA CAACATCTTC ATCGTCTTCG CCATTGTTTT 180

TATCATCACC CGACTGGTCA TCCTGCCCTT CTGGATCCTG CATTGCACCC TGGGTGTACC 240

CACTGGAGCT CTATCCTGCC TTCTTTGGGC TATTACTTCT TTCAATTCCA TGATGGGAGT 300

TCTACAGCTG CTGCATATCT TCTGGGSCTA CCTCATTTTG CGSATGGGCC CACAAGTTCA 360

TAACTGGGAA AGCTGGT 377

(2) INFORMATION FOR SEQ ID NO:55:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 102 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:55:

Met Ala Leu His Asp Ser Ser Asp Tyr Leu Leu Xaa Ser Ala Lys Met
1 5 10 15

Phe Asn Tyr Ala Gly Trp Lys Asn Thr Cys Asn Asn Ile Phe Ile Val
20 25 30

Phe Ala Ile Val Phe Ile Ile Thr Arg Leu Val Ile Leu Pro Phe Trp
35 40 45

Ile Leu His Cys Thr Leu Gly Val Pro Thr Gly Ala Leu Ser Cys Leu
50 55 60

Leu Trp Ala Ile Thr Ser Phe Asn Ser Met Met Gly Val Leu Gln Leu
65 70 75 80

Leu His Ile Phe Trp Xaa Tyr Leu Ile Leu Arg Met Gly Pro Gln Val
85 90 95

His Asn Trp Glu Ser Trp
100

(2) INFORMATION FOR SEQ ID NO:56:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 369 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:56:

AAAAAGTGGG GGCTGTACTG GGGACTGCTC GGATGATNTT TNTTAGTGNT ACTTTTTTCA 60

GCTGTCCCTG TAGCGACAGG TNTAAGATCT GACTGCCTCC TTTTTNTGGC NTCTTCCCCC 120

TTCCNTNTTC TCTTCAGNTA GGCTAGCTGG TTTGGAGTAG AATGGCAACT AATTNTAATT 180

TTTATTTATT AAATATTTGG GGTTTTGGTT TTAAAGCCAG AATTACGGNT AGCACCTAGC 240

ATTTCNGCAG AGGGACCATT TTNGACCNAA ATNTANTNTT NATGGGTTTT TTTTTAAAAT 300

TNAAAGATTA AATNNNAAAT ATTAAATAAA AAAAAAAAAA AAAAAAAAAA AAAAAAAAAG 360

CGCGGCCGC 369

(2) INFORMATION FOR SEQ ID NO:57:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 423 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:57:

GAATTCGGCA CGNNGTGNAA TATAAAAATT TATTTTTAAG TCAAAGTATG CAACAAATAA 60

ACCTACAGAA AACATTTTCC CATCACAATC TGTTGCTTTA CCAAATAATA TTTTGAAAAC 120

ACATTCCTTC AGTCATTATA AAGTTCTTAA AATACAAAAG AAATTAAATC TGTAAGAAAG 180

TCTAGTAGAC CAGATGCTGT TGTCAAGACT TGTATGTTGG TGTTTTTGCT TTCAGTACAT 240

CCCACGCCAT CCACCTCCAC TYCATGCCGC CTTGCCCATA GTAACCTCCA CTGCCTCCAC 300

CACCACGGCC ATAACCACCC AAACCATCAG GAGTACCATA TCCTCCACTG TAATTGTTCC 360

CCATTCCCAT TCTTCCAACT GGATTCCATA GGCCYTCCCT GGATTATTTT TNAAAAGGAA 420

AAA 423

(2) INFORMATION FOR SEQ ID NO:58:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 76 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:58:

Met Leu Leu Ser Arg Leu Val Cys Trp Cys Phe Cys Phe Gln Tyr Ile
1 5 10 15

Pro Arg His Pro Pro Pro Leu His Ala Ala Leu Pro Ile Val Thr Ser
20 25 30

Thr Ala Ser Thr Thr Thr Ala Ile Thr Thr Gln Thr Ile Arg Ser Thr
35 40 45

Ile Ser Ser Thr Val Ile Val Pro His Ser His Ser Ser Asn Trp Ile
50 55 60

Pro Xaa Ala Xaa Pro Gly Leu Phe Xaa Lys Arg Lys
65 70 75

(2) INFORMATION FOR SEQ ID NO:59:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 294 base pairs

(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:59:

TAAAAACCCC TTTTTCCTCN TANGGGTNTA TCATAGGGTC CCGGTNGCTG TCCCAGCAAT 60

TTTNTNGGNG GATCATAAAA TCCTTNGATT TNACTCGTGA NANTTGNGAA GATCTCAATA 120

TACCTATTTA AAAATGTTTT AAGGTACAGG TTTCAGCATA AATGTATTAG TGTAAATTAG 180

ATACNGGGCA AAATGCAGTA AGTTTTTTNTA TATNTAGATA CATAACCCAA TTTAAATTGC 240

CTAAATACAC CGTAAGTTAA CAGTTTAAAC CTACAAACTT AATTAAGCGG CCGC 294

What is claimed is:

1. A composition comprising an isolated protein encoded by a polynucleotide selected from the group consisting of:

(a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:1;

(b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:1 from nucleotide 70 to nucleotide 505;

(c) a polynucleotide comprising the nucleotide sequence of the full length protein coding sequence of clone AP162 deposited under accession number ATCC 98026 ;

(d) a polynucleotide encoding the full length protein encoded by the cDNA insert of clone AP162 deposited under accession number ATCC 98026 ;

(e) a polynucleotide comprising the nucleotide sequence of the mature protein coding sequence of clone AP162 deposited under accession number ATCC 98026 ;

(f) a polynucleotide encoding the mature protein encoded by the cDNA insert of clone AP162 deposited under accession number ATCC 98026 ;

(g) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:2;

(h) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:2 having biological activity;

(i) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(f) above; and

(j) a polynucleotide which encodes a species homologue of the protein of (g) or (h) above.

2. The composition of claim 1, further comprising a pharmaceutically acceptable carrier.

3. A method for preventing, treating or ameliorating a medical condition which comprises administering to a mammalian subject a therapeutically effective amount of a composition of claim 2.

4. A composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence of SEQ ID NO:2;

(b) the amino acid sequence of SEQ ID NO:2 from amino acid 42 to amino acid 61;

(c) fragments of the amino acid sequence of SEQ ID NO:2; and

(d) the amino acid sequence encoded by the cDNA insert of clone AP162 deposited under accession number ATCC 98026;

the protein being substantially free from other mammalian proteins.

5. The composition of claim 4, wherein said protein comprises the amino acid sequence of SEQ ID NO:2.

6. The composition of claim 4, wherein said protein comprises the amino acid sequence of SEQ ID NO:2 from amino acid 42 to amino acid 61.

7. The composition of claim 2, further comprising a pharmaceutically acceptable carrier.

8. A method for preventing, treating or ameliorating a medical condition which comprises administering to a mammalian subject a therapeutically effective amount of a composition of claim 7.

9. A composition comprising an isolated protein encoded by a polynucleotide selected from the group consisting of:

(a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:4;

(b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:4 from nucleotide 230 to nucleotide 791;

(c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:4 from nucleotide 311 to nucleotide 791;

(d) a polynucleotide comprising the nucleotide sequence of the full length protein coding sequence of cl ne AM931 deposited under accession number ATCC 98026 ;

(e) a polynucleotide encoding the full length protein encoded by the cDNA insert of clone AM931 deposited under accession number ATCC 98026 ;

(f) a polynucleotide comprising the nucleotide sequence of the mature protein coding sequence of clone AM931 deposited under accession number ATCC 98026 ;

(g) a polynucleotide encoding the mature protein encoded by the cDNA insert of clone AM931 deposited under accession number ATCC 98026 ;

(h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:5;

(i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:5 having biological activity;

(j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above; and

(k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above.

10. A composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence of SEQ ID NO:5;

(b) the amino acid sequence of SEQ ID NO:5 from amino acid 32 to amino acid 51;

(c) fragments of the amino acid sequence of SEQ ID NO:5; and

(d) the amino acid sequence encoded by the cDNA insert of clone AM931 deposited under accession number ATCC 98026;

the protein being substantially free from other mammalian proteins.

11. A composition comprising an isolated protein encoded by a polynucleotide selected from the group consisting of:

(a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:6;

(b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:6 from nucleotide 14 to nucleotide 491;

(c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:6 from nucleotide 83 t nucleotide 491;

(d) a polynucleotide comprising the nucleotide sequence of the full length protein coding sequence of clone AM610 deposited under accession number ATCC 98026 ;

(e) a polynucleotide encoding the full length protein encoded by the cDNA insert of clone AM610 deposited under accession number ATCC 98026 ;

(f) a polynucleotide comprising the nucleotide sequence of the mature protein coding sequence of clone AM610 deposited under accession number ATCC 98026 ;

(g) a polynucleotide encoding the mature protein encoded by the cDNA insert of clone AM610 deposited under accession number ATCC 98026 ;

(h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:7;

(i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:7 having biological activity;

(j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above; and

(k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above.

12. A composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence of SEQ ID NO:7;

(b) the amino acid sequence of SEQ ID NO:7 from amino acid 31 to amino acid 50;

(c) fragments of the amino acid sequence of SEQ ID NO:7; and

(d) the amino acid sequence encoded by the cDNA insert of clone AM610 deposited under accession number ATCC 98026;

the protein being substantially free from other mammalian proteins.

13. A composition comprising an isolated protein encoded by a polynucleotide selected from the group consisting of:

(a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:9;

(b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:9 from nucleotide 1 to nucleotide 483;

(c) a polynucleotide comprising the nucleotide sequence of the full length protein coding sequence of clone AM340 deposited under accession number ATCC 98026 ;

(d) a polynucleotide encoding the full length protein encoded by the cDNA insert of clone AM340 deposited under accession number ATCC 98026 ;

(e) a polynucleotide comprising the nucleotide sequence of the mature protein coding sequence of clone AM340 deposited under accession number ATCC 98026 ;

(f) a polynucleotide encoding the mature protein encoded by the cDNA insert of clone AM340 deposited under accession number ATCC 98026 ;

(g) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:10;

(h) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:10 having biological activity;

(i) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(f) above; and

(j) a polynucleotide which encodes a species homologue of the protein of (g) or (h) above.

14. A composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence of SEQ ID NO:10;

(b) the amino acid sequence of SEQ ID NO:10 from amino acid 124 to amino acid 143;

(c) fragments of the amino acid sequence of SEQ ID NO:10; and

(d) the amino acid sequence encoded by the cDNA insert of clone AM340 deposited under accession number ATCC 98026;

the protein being substantially free from other mammalian proteins.

15. A composition comprising an isolated protein encoded by a polynucleotide selected from the group consisting of:

(a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:11;

(b) a polynucle tide comprising the nucleotide sequence of SEQ ID NO:11 from nucleotide 15 to nucleotide 462;

(c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:11 from nucleotide 87 to nucleotide 462;

(d) a polynucleotide comprising the nucleotide sequence of the full length protein coding sequence of clone AM282 deposited under accession number ATCC 98026 ;

(e) a polynucleotide encoding the full length protein encoded by the cDNA insert of clone AM282 deposited under accession number ATCC 98026 ;

(f) a polynucleotide comprising the nucleotide sequence of the mature protein coding sequence of clone AM282 deposited under accession number ATCC 98026 ;

(g) a polynucleotide encoding the mature protein encoded by the cDNA insert of clone AM282 deposited under accession number ATCC 98026 ;

(h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:12;

(i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:12 having biological activity;

(j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above; and

(k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above.

16. A composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence of SEQ ID NO:12;

(b) the amino acid sequence of SEQ ID NO:12 from amino acid 28 to amino acid 47;

(c) fragments of the amino acid sequence of SEQ ID NO:12; and

(d) the amino acid sequence encoded by the cDNA insert of clone AM282 deposited under accession number ATCC 98026;

the protein being substantially free from other mammalian proteins.

17. A composition c mprising an isolated protein encoded by a polynucleotide selected from the group consisting of:

(a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:14;

(b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:14 from nucleotide 185 to nucleotide 519;

(c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:14 from nucleotide 260 to nucleotide 519;

(d) a polynucleotide comprising the nucleotide sequence of the full length protein coding sequence of clone AK647 deposited under accession number ATCC 98026 ;

(e) a polynucleotide encoding the full length protein encoded by the cDNA insert of clone AK647 deposited under accession number ATCC 98026 ;

(f) a polynucleotide comprising the nucleotide sequence of the mature protein coding sequence of clone AK647 deposited under accession number ATCC 98026 ;

(g) a polynucleotide encoding the mature protein encoded by the cDNA insert of clone AK647 deposited under accession number ATCC 98026 ;

(h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:15;

(i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:15 having biological activity;

(j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above; and

(k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above.

18. A composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence of SEQ ID NO:15;

(b) the amino acid sequence of SEQ ID NO:15 from amino acid 27 to amino acid 46;

(c) fragments of the amino acid sequence of SEQ ID NO:15; and

(d) the amino acid sequence encoded by the cDNA insert of clone AK647 deposited under accession number ATCC 98026;

the protein being substantially free from other mammalian proteins.

19. A composition comprising an isolated protein encoded by a polynucleotide selected from the group consisting of:

(a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:17;

(b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:17 from nucleotide 257 to nucleotide 536;

(c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:17 from nucleotide 329 to nucleotide 536;

(d) a polynucleotide comprising the nucleotide sequence of the full length protein coding sequence of clone AK583 deposited under accession number ATCC 98026 ;

(e) a polynucleotide encoding the full length protein encoded by the cDNA insert of clone AK583 deposited under accession number ATCC 98026 ;

(f) a polynucleotide comprising the nucleotide sequence of the mature protein coding sequence of clone AK583 deposited under accession number ATCC 98026 ;

(g) a polynucleotide encoding the mature protein encoded by the cDNA insert of clone AK583 deposited under accession number ATCC 98026 ;

(h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:18;

(i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:18 having biological activity;

(j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above; and

(k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above.

20. A composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence of SEQ ID NO:18;

(b) the amino acid sequence of SEQ ID NO:18 from amino acid 14 to amino acid 33;

(c) fragments of the amino acid sequence of SEQ ID NO:18; and

(d) the amino acid sequence encoded by the cDNA insert of clone AK583 deposited under accession number ATCC 98026;

the protein being substantially free from other mammalian proteins.

21. A composition comprising an isolated protein encoded by a polynucleotide selected from the group consisting of:

(a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:20;

(b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:20 from nucleotide 179 to nucleotide 476;

(c) a polynucleotide comprising the nucleotide sequence of the full length protein coding sequence of clone AK533 deposited under accession number ATCC 98026 ;

(d) a polynucleotide encoding the full length protein encoded by the cDNA insert of clone AK533 deposited under accession number ATCC 98026 ;

(e) a polynucleotide comprising the nucleotide sequence of the mature protein coding sequence of clone AK533 deposited under accession number ATCC 98026 ;

(f) a polynucleotide encoding the mature protein encoded by the cDNA insert of clone AK533 deposited under accession number ATCC 98026 ;

(g) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:21;

(h) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:21 having biological activity;

(i) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(f) above; and

(j) a polynucleotide which encodes a species homologue of the protein of (g) or (h) above.

22. A composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence of SEQ ID NO:21;

(b) the amino acid sequence of SEQ ID NO:21 from amino acid 35 to amino acid 57;

(c) fragments of the amino acid sequence of SEQ ID NO:21; and

(d) the amino acid sequence encoded by the cDNA insert of clone AK533 deposited under accession number ATCC 98026;

the protein being substantially free from other mammalian proteins.

23. A composition comprising an isolated protein encoded by a polynucleotide selected from the group consisting of:

(a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:23;

(b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:23 from nucleotide 220 to nucleotide 612;

(c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:23 from nucleotide 328 to nucleotide 612;

(d) a polynucleotide comprising the nucleotide sequence of the full length protein coding sequence of clone AK296 deposited under accession number ATCC 98026 ;

(e) a polynucleotide encoding the full length protein encoded by the cDNA insert of clone AK296 deposited under accession number ATCC 98026 ;

(f) a polynucleotide comprising the nucleotide sequence of the mature protein coding sequence of clone AK296 deposited under accession number ATCC 98026 ;

(g) a polynucleotide encoding the mature protein encoded by the cDNA insert of clone AK296 deposited under accession number ATCC 98026 ;

(h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:24;

(i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:24 having biological activity;

(j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above; and

(k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above.

24. A composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence of SEQ ID NO:24;

(b) the amino acid sequence of SEQ ID NO:24 from amino acid 81 to amino acid 90;

(c) fragments of the amino acid sequence of SEQ ID NO:24; and

(d) the amino acid sequence encoded by the cDNA insert of clone AK296 deposited under accession number ATCC 98026;

the protein being substantially free from other mammalian proteins.

25. A composition comprising an isolated protein encoded by a polynucleotide selected from the group consisting of:

(a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:26;

(b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:26 from nucleotide 58 to nucleotide 655;

(c) a polynucleotide comprising the nucleotide sequence of the full length protein coding sequence of clone H617 deposited under accession number ATCC 98026 ;

(d) a polynucleotide encoding the full length protein encoded by the cDNA insert of clone H617 deposited under accession number ATCC 98026 ;

(e) a polynucleotide comprising the nucleotide sequence of the mature protein coding sequence of clone H617 deposited under accession number ATCC 98026 ;

(f) a polynucleotide encoding the mature protein encoded by the cDNA insert of clone H617 deposited under accession number ATCC 98026 ;

(g) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:27;

(h) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:27 having biological activity;

(i) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(f) above; and

(j) a polynucleotide which encodes a species homologue of the protein of (g) or (h) above.

26. A composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence of SEQ ID NO:27;

(b) the amin acid sequence of SEQ ID NO:27 from amino acid 65 to amino acid 84;

(c) fragments of the amino acid sequence of SEQ ID NO:27; and

(d) the amino acid sequence encoded by the cDNA insert of clone H617 deposited under accession number ATCC 98026;

the protein being substantially free from other mammalian proteins.

27. A composition comprising an isolated protein encoded by a polynucleotide selected from the group consisting of:

(a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:29;

(b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:29 from nucleotide 14 to nucleotide 391;

(c) a polynucleotide comprising the nucleotide sequence of the full length protein coding sequence of clone BB9 deposited under accession number ATCC 98026 ;

(d) a polynucleotide encoding the full length protein encoded by the cDNA insert of clone BB9 deposited under accession number ATCC 98026 ;

(e) a polynucleotide comprising the nucleotide sequence of the mature protein coding sequence of clone BB9 deposited under accession number ATCC 98026 ;

(f) a polynucleotide encoding the mature protein encoded by the cDNA insert of clone BB9 deposited under accession number ATCC 98026 ;

(g) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:30;

(h) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:30 having biological activity;

(i) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(f) above; and

(j) a polynucleotide which encodes a species homologue of the protein of (g) or (h) above.

28. A composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence of SEQ ID NO:30;

(b) the amino acid sequence of SEQ ID NO:30 from amino acid 75 to amino acid 94;

(c) fragments of the amino acid sequence of SEQ ID NO:30; and

(d) the amino acid sequence encoded by the cDNA insert of clone BB9 deposited under accession number ATCC 98026;

the protein being substantially free from other mammalian proteins.

29. A composition comprising an isolated protein encoded by a polynucleotide selected from the group consisting of:

(a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:32;

(b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:32 from nucleotide 61 to nucleotide 514;

(c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:32 from nucleotide 115 to nucleotide 514;

(d) a polynucleotide comprising the nucleotide sequence of the full length protein coding sequence of clone AW191 deposited under accession number ATCC 98026 ;

(e) a polynucleotide encoding the full length protein encoded by the cDNA insert of clone AW191 deposited under accession number ATCC 98026 ;

(f) a polynucleotide comprising the nucleotide sequence of the mature protein coding sequence of clone AW191 deposited under accession number ATCC 98026 ;

(g) a polynucleotide encoding the mature protein encoded by the cDNA insert of clone AW191 deposited under accession number ATCC 98026 ;

(h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:33;

(i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:33 having biological activity;

(j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above; and

(k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above.

30. A composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence of SEQ ID NO:33;

(b) the amino acid sequence of SEQ ID NO:33 from amino acid 24 to amino acid 43;

(c) fragments of the amino acid sequence of SEQ ID NO:33; and

(d) the amino acid sequence encoded by the cDNA insert of clone AW191 deposited under accession number ATCC 98026;

the protein being substantially free from other mammalian proteins.

31. A composition comprising an isolated protein encoded by a polynucleotide selected from the group consisting of:

(a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:35;

(b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:35 from nucleotide 180 to nucleotide 525;

(c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:35 from nucleotide 339 to nucleotide 525;

(d) a polynucleotide comprising the nucleotide sequence of the full length protein coding sequence of clone AT211 deposited under accession number ATCC 98026 ;

(e) a polynucleotide encoding the full length protein encoded by the cDNA insert of clone AT211 deposited under accession number ATCC 98026 ;

(f) a polynucleotide comprising the nucleotide sequence of the mature protein coding sequence of clone AT211 deposited under accession number ATCC 98026 ;

(g) a polynucleotide encoding the mature protein encoded by the cDNA insert of clone AT211 deposited under accession number ATCC 98026 ;

(h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:36;

(i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:36 having biological activity;

(j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above; and

(k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above.

32. A composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence of SEQ ID NO:36;

(b) the amino acid sequence of SEQ ID NO:36 from amino acid 1 to amino acid 20;

(c) fragments of the amino acid sequence of SEQ ID NO:36; and

(d) the amino acid sequence encoded by the cDNA insert of clone AT211 deposited under accession number ATCC 98026;

the protein being substantially free from other mammalian proteins.

33. A composition comprising an isolated protein encoded by a polynucleotide selected from the group consisting of:

(a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:38;

(b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:38 from nucleotide 225 to nucleotide 677;

(c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:38 from nucleotide 390 to nucleotide 677;

(d) a polynucleotide comprising the nucleotide sequence of the full length protein coding sequence of clone AT205 deposited under accession number ATCC 98026 ;

(e) a polynucleotide encoding the full length protein encoded by the cDNA insert of clone AT205 deposited under accession number ATCC 98026 ;

(f) a polynucleotide comprising the nucleotide sequence of the mature protein coding sequence of clone AT205 deposited under accession number ATCC 98026 ;

(g) a polynucleotide encoding the mature protein encoded by the cDNA insert of clone AT205 deposited under accession number ATCC 98026 ;

(h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:39;

(i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:39 having biological activity;

(j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above; and

(k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above.

34. A composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence of SEQ ID NO:39;

(b) the amino acid sequence of SEQ ID NO:39 from amino acid 6 to amino acid 25;

(c) fragments of the amino acid sequence of SEQ ID NO:39; and

(d) the amino acid sequence encoded by the cDNA insert of clone AT205 deposited under accession number ATCC 98026;

the protein being substantially free from other mammalian proteins.

35. A composition comprising an isolated protein encoded by a polynucleotide selected from the group consisting of:

(a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:40;

(b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:40 from nucleotide 128 to nucleotide 508;

(c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:40 from nucleotide 200 to nucleotide 508;

(d) a polynucleotide comprising the nucleotide sequence of the full length protein coding sequence of clone AS34 deposited under accession number ATCC 98026 ;

(e) a polynucleotide encoding the full length protein encoded by the cDNA insert of clone AS34 deposited under accession number ATCC 98026 ;

(f) a polynucleotide comprising the nucleotide sequence of the mature protein coding sequence of clone AS34 deposited under accession number ATCC 98026 ;

(g) a polynucleotide encoding the mature protein encoded by the cDNA insert of clone AS34 deposited under accession number ATCC 98026 ;

(h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:41;

(i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:41 having biological activity;

(j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above; and

(k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above.

36. A composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence of SEQ ID NO:41;

(b) the amino acid sequence of SEQ ID NO:41 from amino acid 27 to amino acid 46;

(c) fragments of the amino acid sequence of SEQ ID NO:41; and

(d) the amino acid sequence encoded by the cDNA insert of clone AS34 deposited under accession number ATCC 98026;

the protein being substantially free from other mammalian proteins.

37. A composition comprising an isolated protein encoded by a polynucleotide selected from the group consisting of:

(a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:43;

(b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:43 from nucleotide 23 to nucleotide 676;

(c) a polynucleotide comprising the nucleotide sequence of the full length protein coding sequence of clone AS32 deposited under accession number ATCC 98026 ;

(d) a polynucleotide encoding the full length protein encoded by the cDNA insert of clone AS32 deposited under accession number ATCC 98026 ;

(e) a polynucleotide comprising the nucleotide sequence of the mature protein coding sequence of clone AS32 deposited under accession number ATCC 98026 ;

(f) a polynucleotide encoding the mature protein encoded by the cDNA insert of clone AS32 deposited under accession number ATCC 98026 ;

(g) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:44;

(h) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:44 having biological activity;

(i) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(f) above; and

(j) a polynucleotide which encodes a species homologue of the protein of (g) or (h) above.

38. A composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence of SEQ ID NO:44;

(b) the amino acid sequence of SEQ ID NO:44 from amino acid 78 to amino acid 97;

(c) fragments of the amino acid sequence of SEQ ID NO:44; and

(d) the amino acid sequence encoded by the cDNA insert of clone AS32 deposited under accession number ATCC 98026;

the protein being substantially free from other mammalian proteins.

39. A composition comprising an isolated protein encoded by a polynucleotide selected from the group consisting of:

(a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:46;

(b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:46 from nucleotide 132 to nucleotide 479;

(c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:46 from nucleotide 201 to nucleotide 479;

(d) a polynucleotide comprising the nucleotide sequence of the full length protein coding sequence of clone AR260 deposited under accession number ATCC 98026 ;

(e) a polynucleotide encoding the full length protein encoded by the cDNA insert of clone AR260 deposited under accession number ATCC 98026 ;

(f) a polynucleotide comprising the nucleotide sequence of the mature protein coding sequence of clone AR260 deposited under accession number ATCC 98026 ;

(g) a polynucleotide encoding the mature protein encoded by the cDNA insert of clone AR260 deposited under accession number ATCC 98026 ;

(h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:47;

(i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:47 having biological activity;

(j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above; and

(k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above.

40. A composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence of SEQ ID NO:47;

(b) the amino acid sequence of SEQ ID NO:47 from amino acid 40 to amino acid 59;

(c) fragments of the amino acid sequence of SEQ ID NO:47; and

(d) the amino acid sequence encoded by the cDNA insert of clone AR260 deposited under accession number ATCC 98026;

the protein being substantially free from other mammalian proteins.

41. A composition comprising an isolated protein encoded by a polynucleotide selected from the group consisting of:

(a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:50;

(b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:50 from nucleotide 1 to nucleotide 332;

(c) a polynucleotide comprising the nucleotide sequence of the full length protein coding sequence of clone K640 deposited under accession number ATCC 98026 ;

(d) a polynucleotide encoding the full length protein encoded by the cDNA insert of clone K640 deposited under accession number ATCC 98026 ;

(e) a polynucleotide comprising the nucleotide sequence of the mature protein coding sequence of clone K640 deposited under accession number ATCC 98026 ;

(f) a polynucleotide encoding the mature protein encoded by the cDNA insert of clone K640 deposited under accession number ATCC 98026 ;

(g) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:51;

(h) a polynucleotide encoding a protein comprising a fragment f the amino acid sequence of SEQ ID NO:51 having biological activity;

(i) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(f) above; and

(j) a polynucleotide which encodes a species homologue of the protein of (g) or (h) above.

42. A composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence of SEQ ID NO:51;

(b) the amino acid sequence of SEQ ID NO:51 from amino acid 11 to amino acid 30;

(c) fragments of the amino acid sequence of SEQ ID NO:51; and

(d) the amino acid sequence encoded by the cDNA insert of clone K640 deposited under accession number ATCC 98026;

the protein being substantially free from other mammalian proteins.

43. A composition comprising an isolated protein encoded by a polynucleotide selected from the group consisting of:

(a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:54;

(b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:54 from nucleotide 71 to nucleotide 377;

(c) a polynucleotide comprising the nucleotide sequence of the full length protein coding sequence of clone K39 deposited under accession number ATCC 98026 ;

(d) a polynucleotide encoding the full length protein encoded by the cDNA insert of clone K39 deposited under accession number ATCC 98026 ;

(e) a polynucleotide comprising the nucleotide sequence of the mature protein coding sequence of clone K39 deposited under accession number ATCC 98026 ;

(f) a polynucleotide encoding the mature protein encoded by the cDNA insert of clone K39 deposited under accession number ATCC 98026 ;

(g) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:55;

(h) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:55 having biological activity;

(i) a p lynucleotide which is an allelic variant of a polynucleotide of (a)-(f) above; and

(j) a polynucleotide which encodes a species homologue of the protein of (g) or (h) above.

44. A composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence of SEQ ID NO:55;

(b) the amino acid sequence of SEQ ID NO:55 from amino acid 62 to amino acid 81;

(c) fragments of the amino acid sequence of SEQ ID NO:55; and

(d) the amino acid sequence encoded by the cDNA insert of clone K39 deposited under accession number ATCC 98026;

the protein being substantially free from other mammalian proteins.

45. A composition comprising an isolated protein encoded by a polynucleotide selected from the group consisting of:

(a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:57;

(b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:57 from nucleotide 194 to nucleotide 423;

(c) a polynucleotide comprising the nucleotide sequence of the full length protein coding sequence of clone AT319 deposited under accession number ATCC 98026 ;

(d) a polynucleotide encoding the full length protein encoded by the cDNA insert of clone AT319 deposited under accession number ATCC 98026 ;

(e) a polynucleotide comprising the nucleotide sequence of the mature protein coding sequence of clone AT319 deposited under accession number ATCC 98026 ;

(f) a polynucleotide encoding the mature protein encoded by the cDNA insert of clone AT319 deposited under accession number ATCC 98026 ;

(g) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:58;

(h) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:58 having biological activity;

(i) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(f) above; and

(j) a polynucleotide which encodes a species homologue of the protein of (g) or (h) above.

46. A composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

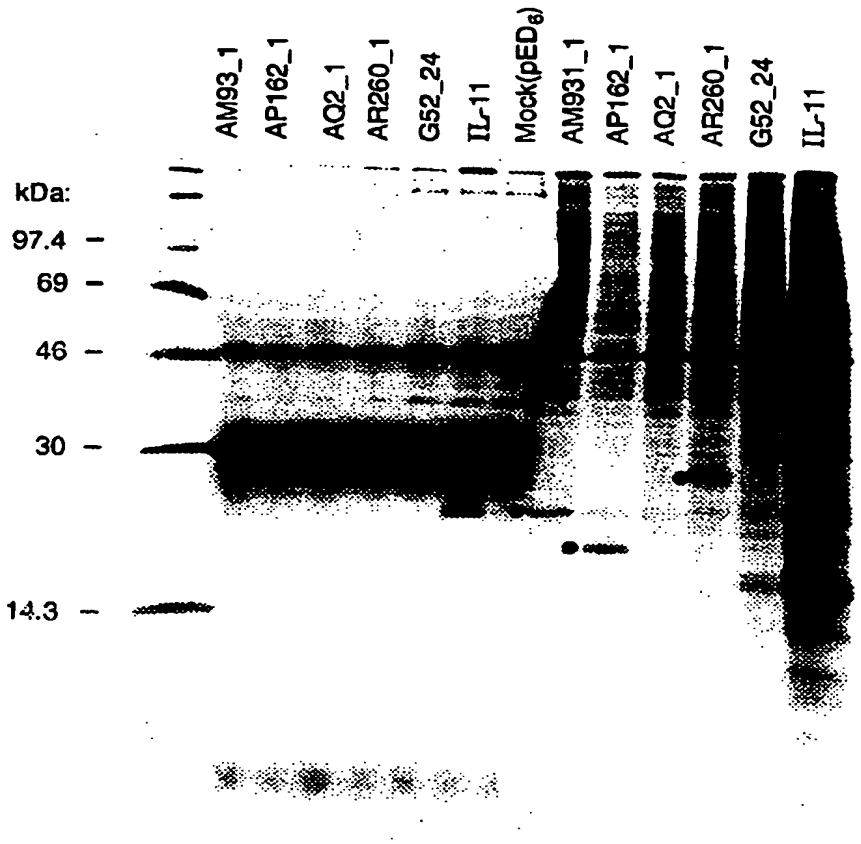
(a) the amino acid sequence of SEQ ID NO:58;

(b) the amino acid sequence of SEQ ID NO:58 from amino acid 2 to amino acid 21;

(c) fragments of the amino acid sequence of SEQ ID NO:58; and

(d) the amino acid sequence encoded by the cDNA insert of clone AT319 deposited under accession number ATCC 98026;

the protein being substantially free from other mammalian proteins.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69
46
30
14.3

Fig. 1

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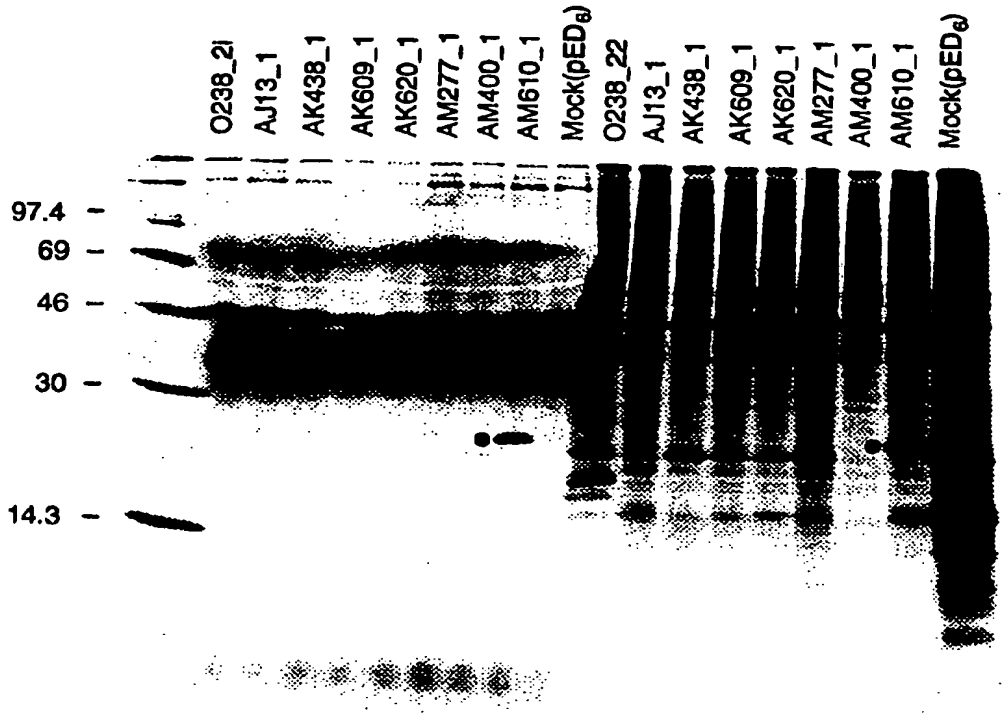
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AK609_1
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AM610_1
Mock(pED6)
97.4
69
46
30
14.3

Fig. 2

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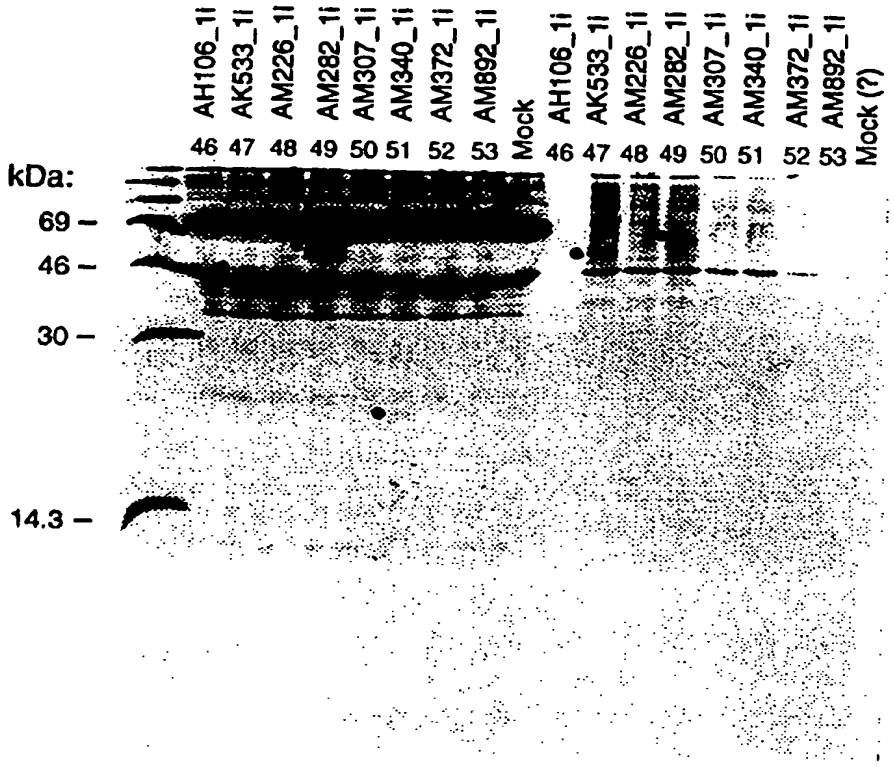


Fig. 3

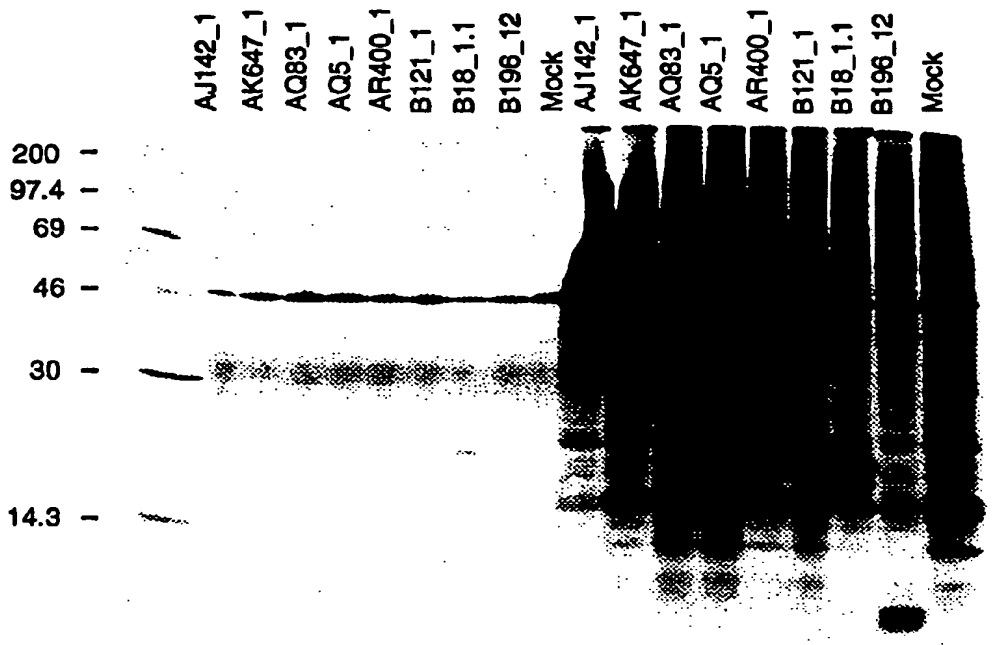
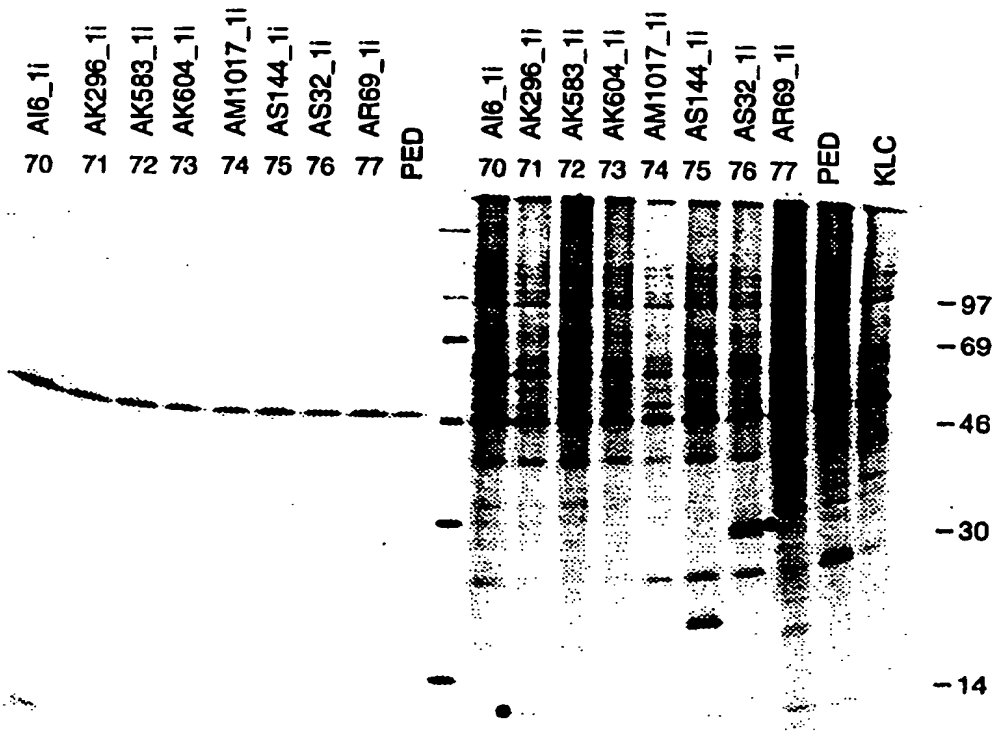


Fig. 4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AM1017_1i
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97
69
46
30
14

Fig. 5

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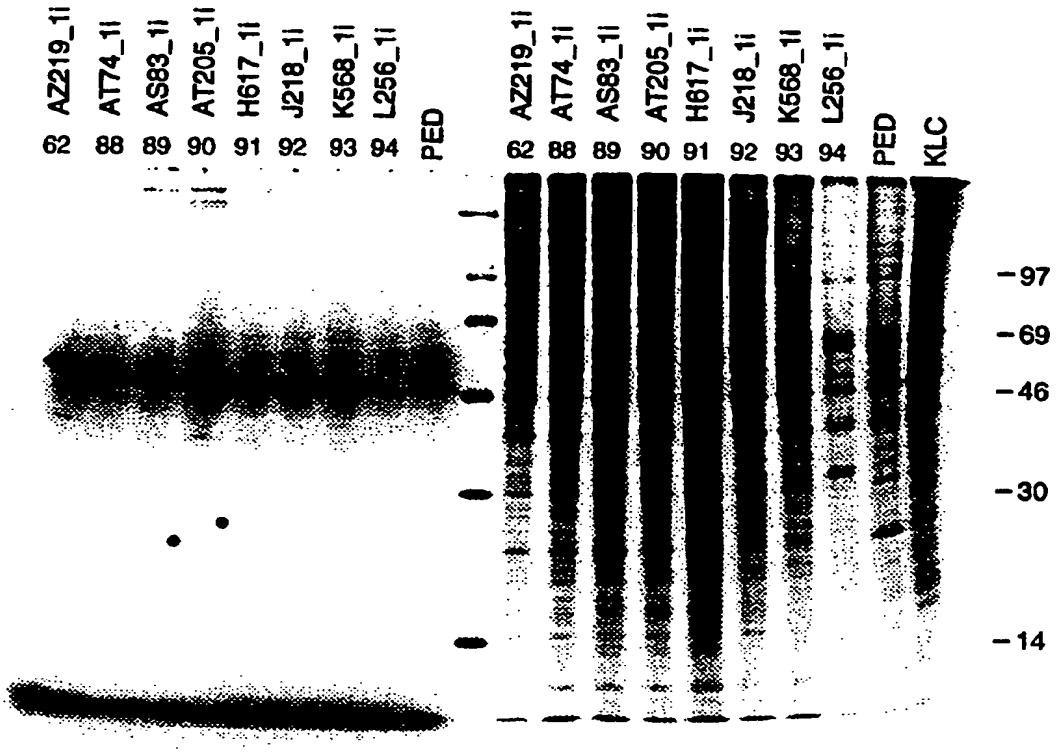
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97
69
46
30
14

Fig. 6

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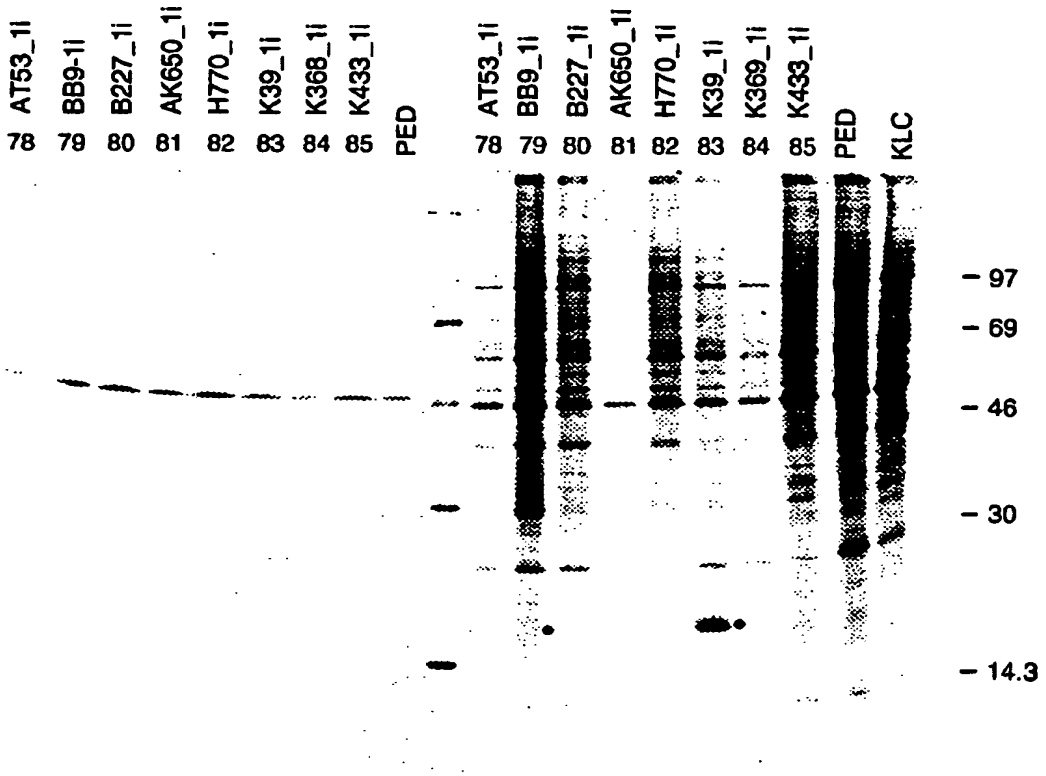
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97
69
46
30
14.3

Fig. 7

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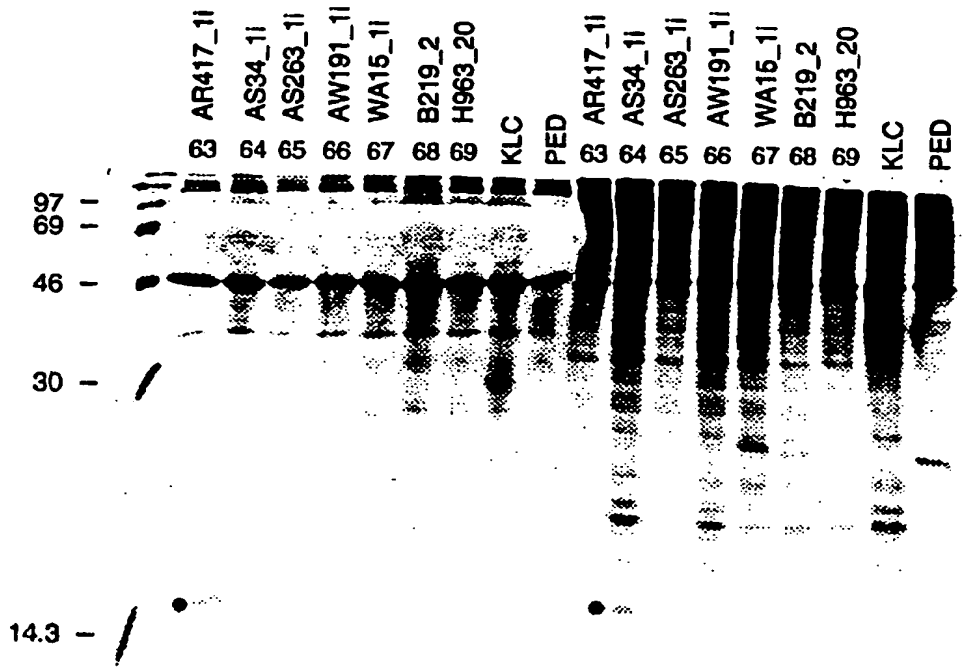
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46
30
14.3

Fig. 8

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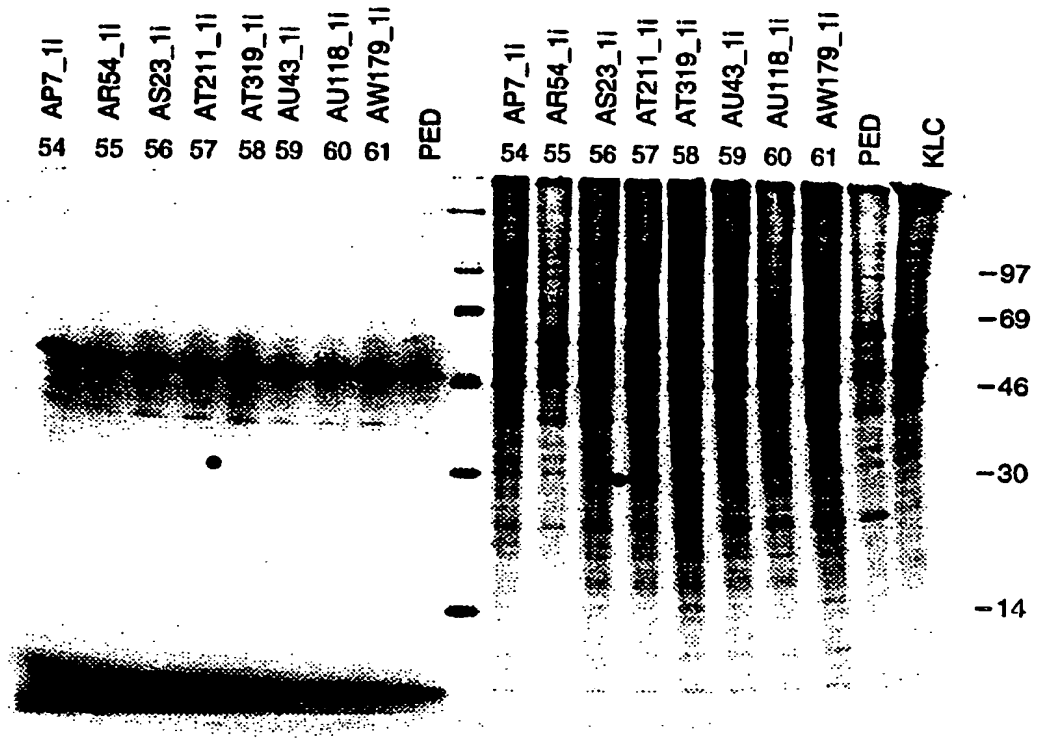
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AU43_1i
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-97
-69
-46
-30
-14

Fig. 9

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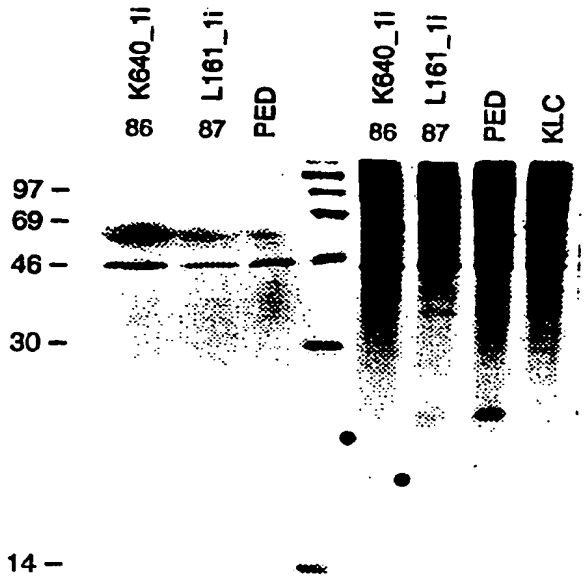
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PED
KLC
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87
86
87
97 –
69 –
46 –
30 –
14 –

Fig. 10

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